In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 17-1553V

Filed: June 16, 2023

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ELAINE CLARK,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

* *

Phyllis Widman, Widman Law Firm, LLC, Northfield, NJ, for Petitioner
Ryan Pyles, U.S. Department of Justice, Washington, DC, for Respondent

DECISION ON ENTITLEMENT[1]

Oler, Special Master:

On October 18, 2017, Elaine Clark ("Petitioner") filed a petition for compensation under the National Vaccine Injury Compensation Program, 42 U.S.C. § 300aa-10, *et seq*.[2] (the "Vaccine Act" or "Program"). The petition alleges that Petitioner developed "significant aggravation/exacerbation of arthritis, rheumatoid arthritis with associated polyneuropathy/small fiber neuropathy, exacerbation of carpal tunnel syndrome, and a left shoulder injury" as a result of the influenza ("flu") vaccine she received on December 6, 2015. Pet. at 1, ECF No. 1. Petitioner

[1] Because this Decision contains a reasoned explanation for the action in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the Decision will be available to anyone with access to the internet.** In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, I agree that the identified material fits within this definition, I will redact such material from public access.

[2] National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

later clarified that she was alleging the flu vaccine caused her to develop rheumatoid arthritis ("RA"). ECF No. 41.

Upon review of the evidence in this case, I find that Petitioner has failed to preponderantly demonstrate that the flu vaccine can cause RA or that it did so in this case. The petition is accordingly dismissed.

I. Procedural History

Petitioner filed her petition on October 18, 2017. Pet. at 1. She filed medical records in support of her petition on November 1, 2017 (Exs. 1, 3-9), November 8, 2017 (Ex. 10), November 22, 2017 (Ex. 11), January 31, 2018 (Exs. 12-14), and April 11, 2018 (Exs. 15-18).

Respondent filed his Rule 4(c) report on July 6, 2018, recommending that entitlement be denied. ECF No. 26 ("Resp't's Rep.") at 1.

After that, the parties each filed an expert report from a rheumatologist; Petitioner filed a report from Dr. Arthur Brawer and Respondent filed a report from Dr. Merhdad Matloubian. Ex. 19; Ex. A.

I held a status conference on September 5, 2019. During my discussion with the parties, I confirmed with Petitioner's counsel that Petitioner's alleged injury is RA. Counsel indicated that this was the case.[3] *See* ECF No. 41. I also informed Petitioner's counsel that it will be "difficult for Petitioner to succeed under the current theory presented by Dr. Brawer. Specifically, I am not convinced Petitioner can establish that an onset of RA within 24 hours following vaccination represents a medically feasible time frame." *Id.* I ordered Petitioner to file a responsive expert report both responding to Respondent's expert and addressing this issue. *Id.*

Petitioner filed a second expert report from Dr. Brawer on September 18, 2019. Ex. 20.

I held a status conference on November 20, 2019. During that conference, I told Petitioner's counsel that

> Dr. Brawer's latest expert report did not fully address my question regarding how rheumatoid arthritis ("RA") can develop within 24 hours of vaccination. Dr. Brawer proposed a theory of molecular mimicry in his prior expert report to explain why vaccines have caused a wide variety of autoimmune diseases. In this case, Dr. Brawer did not address medical feasibility of onset of RA within 24 hours of the flu vaccination under his molecular mimicry theory, as it relates to *Althen* prong 3. Specifically, he did not explain how it is medically plausible for the immune response, that is a central component of the autoimmune process that causes RA, to occur so quickly.

[3] Based on this assertion, I have not analyzed whether the flu vaccine caused Petitioner to develop any injury other than RA.

ECF No. 43.

Petitioner filed three individual expert reports from Dr. Brawer on January 29, 2020. Exs. 21, 22, 23. Respondent filed a responsive report from Dr. Matloubian on March 30, 2020. Ex. C. Petitioner filed a sixth expert report from Dr. Brawer on April 22, 2020. Ex. 27.

I held a status conference on April 24, 2020. I spoke with the parties about scheduling an entitlement hearing and asked them to submit their availability to chambers. ECF No. 53. Based on the parties' submissions, I scheduled an entitlement hearing for August 24, 2021. *See* Scheduling Order dated 5/1/2020.

The parties filed prehearing briefs on July 27 and August 9, 2021. ECF Nos. 62, 66.

I conducted an entitlement hearing via Zoom on August 24, 2021. Petitioner presented testimony from herself and Dr. Brawer. Respondent presented testimony from Dr. Matloubian.

After the hearing, the parties each filed a supplemental expert report and additional medical literature addressing an issue raised at the entitlement hearing (whether synovitis and erosion are common findings in end-state osteoarthritis). Exs. 37-53; Ex. D; Ex. D, Tab 1.

Subsequently, the parties submitted post-hearing briefs. ECF Nos. 92, 93, 94. Both Petitioner and Respondent indicated that the record was complete on June 21, 2022. ECF No. 95. This matter is now ripe for an adjudication.

II. Medical Records

A. Relevant Pre-Vaccination History

On June 6, 2013, Petitioner saw orthopedist Thomas E. Hoerner, MD, for an evaluation of left knee pain that occasionally radiated up to her hip and down to her ankle. Ex. 4 at 71-72. Petitioner also reported muscle aches, muscle weakness, arthralgias, and joint pain. Ex. 6 at 50. Petitioner had been on "long-time chiropractic manipulation" and Dr. Hoerner's impression was of "calcifying tendinitis of shoulder" (location not specified), joint pain in the pelvic area and thigh, and "disorders of bursae and tendons in shoulder region, unspecified." Ex. 4 at 72. Petitioner reported that she was considering surgery for her left knee arthritis the following September. *Id.*

On November 4, 2013, Petitioner saw her primary care provider, Joseph Gurka, DO, for a follow-up to her right knee replacement surgery. Ex. 4 at 6. Petitioner reported that her left knee might also need surgery soon. *Id.*

On August 6, 2015, Petitioner saw Dr. Hoerner to schedule her left knee replacement surgery. Ex. 4 at 86-87. Dr. Hoerner's impression was of hip and knee pain, "bursitis of shoulder," and "calcific tendinitis of shoulder." *Id.* at 87. On November 4, 2015, Petitioner underwent left knee replacement surgery. Ex. 6 at 5. Dr. Hoerner's notes on the knee replacement procedure reflect "significant bone loss and erosion in the lateral tibial plateau." Ex. 11 at 45. The post-operative pathology report notes that the bone and tissue sample collected during the procedure

contained "[b]ony and cartilaginous fragments with degenerative change, synovial fragments with proliferative synovitis."[4] *Id.* at 47. During a follow-up appointment with Dr. Gurka on November 24, 2015, Petitioner exhibited mild swelling in her left ankle. Ex. 4 at 15.

B. Post-Vaccination History

On December 6, 2015, Petitioner, then 74 years of age, received the allegedly causal flu vaccination in her left arm. Ex. 1 at 1-2.

On December 15, 2015, Petitioner saw Dr. Hoerner for a follow-up to her left knee replacement. Ex. 6 at 43-46. He noted that Petitioner's knee was doing well, but that "her chief complaint is really her ankle and foot pain" *Id.* at 45. In addition, he noted that she "had to get off the walker because of bilateral shoulder pain" and that "she has difficulty elevating the left more than the right." *Id.* There was no documentation of wrist or hand pain by Dr. Hoerner at this visit. Dr. Hoerner also did not mention her flu vaccination. He suspected possible polymyalgia rheumatica (PMR) and ordered blood tests. *Id.* The results showed a normal inflammatory marker and erythrocyte sedimentation rate ("ESR")[5] of 10 on December 15, 2015, making PMR less likely. Ex. 6 at 87.

At her first physical therapy ("PT") appointment on December 12, 2015, Petitioner complained of "increased sh[oulder] & wrist pain." Ex. 5 at 7.

On December 28, 2015, Dr. Gurka evaluated Petitioner for "bilateral shoulder, wrist, and pain [sic] since she has stopped using her crutches since her knee surgery." Ex. 4 at 16. He noted that Petitioner had a mechanical fall on her left side the previous week and that x-rays had shown no fractures. Ex. 4 at 16. On physical exam, he noted reduced range of motion in her shoulders as well as "edema"[6] on bilateral "upper extremities." *Id.* at 17. His assessment was pain in Petitioner's shoulders and left knee, and he recommended follow up with orthopedics. *Id.* at 16.

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[4] Synovitis is "inflammation of a synovial membrane [of a joint]; it is usually painful, particularly on motion, and is characterized by a fluctuating swelling due to effusion within a synovial sac." DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=48576 (last visited on Apr. 25, 2023) (hereinafter "DORLAND'S").

[5] Erythrocyte sedimentation rate is "the rate at which [red blood cells] precipitate out from a well-mixed specimen of venous blood…[A]n increase in rate is usually due to elevated levels of plasma proteins, especially fibrinogen and immunoglobulins...It is increased in monoclonal gammopathy, hypergammaglobulinemia due to inflammatory disease, hyperfibrinogenemia, active inflammatory disease, and anemia." DORLAND'S, https://www.dorlandsonline.com/dorland/definition?id=102146 (last visited on Apr. 24, 2013).

[6] Edema is "the presence of abnormally large amounts of fluid in the intercellular tissue spaces of the body, usually referring to subcutaneous tissues. It may be localized (as from venous obstruction, lymphatic obstruction, or increased vascular permeability) or systemic (as from heart failure or renal disease)." DORLAND'S, https://www.dorlandsonline.com/dorland/definition?id=15589 (last visited on June 2, 2023).

On January 6, 2016, Petitioner saw Peter Shoukimas, PA-C, for an orthopedics follow-up. Ex. 6 at 39-43. He noted that Petitioner complained of "pain in the shoulders with limited range of motion due to discomfort and numbness and tingling in the ulnar nerve distribution of both hands." *Id.* at 41. PA Shoukimas added that "the patient has found that since her surgery for total knee replacement on the left and the use of crutches that this is when the pain occurred and has become somewhat worse." *Id.* His impression was of bursitis of shoulder, calcific tendinitis of shoulder, and PMR. *Id.* at 42.

On January 14, 2016, Petitioner returned to Dr. Hoerner. Ex. 6 at 38. Petitioner stated that she had experienced "sudden onset of right upper extremity pain" on December 6, 2015, the day she received the flu vaccine. *Id.* She stated that her shoulder pain was disrupting her sleep and that "any attempt to elevate the shoulder" would cause pain. *Id.* Petitioner also complained of numbness in the ring and little fingers of her right hand. *Id.*

On January 21, 2016, Petitioner began attending physical therapy for bilateral bursitis and bilateral shoulder pain. Ex. 5 at 32. On January 27, 2016, Petitioner underwent nerve conduction velocity testing via electromyography ("EMG"). Ex. 4 at 51-54. The results were abnormal, showing bilateral median mononeuropathy at the wrists (Carpal Tunnel syndrome) and mild, right ulnar mononeuropathy at the ulnar groove (Cubital Tunnel). *Id.* at 54. The study showed no evidence of bilateral cervical radiculopathy. *Id.*

On January 29, 2016, Petitioner was evaluated by Joshua Philbrick, MD, an associate of Dr. Hoerner, for "bilateral shoulder pain and bilateral hand numbness and tingling." Ex. 6 at 31-35. He noted that Petitioner's pain had begun on December 6, 2015, and that Petitioner "attribute[d] her shoulder pain to the flu shot and the crutches" that she used after her knee replacement surgery. *Id.* at 34. On physical exam of Petitioner's hands, Dr. Philbrick noted some evidence of osteoarthritis in multiple small joints of both of her hands but did not document any joint swelling or hand edema. *Id.* His impression, based on EMG findings was "bilateral carpal tunnel, moderate on the right, mild on the left" as well as "right mild cubital tunnel" in addition to "bilateral shoulder impingement and rotator cuff tendinitis." *Id.*

On physical examination on February 27, 2016, Dr. Gurka noted that Petitioner had bilateral edema of the hands and feet. Ex. 11 at 36. Blood tests performed on February 29, 2016, showed an elevated ESR of 41 (normal <30) and a negative anti-nuclear antibody ("ANA").[7] *Id.* at 21, 23.

On March 11, 2016, Petitioner underwent additional blood tests. Ex. 6 at 85-86. The results showed elevated inflammatory markers, including an ESR of 67 (normal <40), and C-reactive protein ("CRP") of 22.9 (normal <4.9), as well as a positive rheumatoid factor of 42.4 and a

[7] Antinuclear antibodies are "antibodies directed against nuclear antigens; ones against a variety of different antigens are almost invariably found in systemic lupus erythematosus and are frequently found in rheumatoid arthritis, scleroderma (systemic sclerosis), Sjögren syndrome, and mixed connective tissue disease." DORLAND'S, https://www.dorlandsonline.com/dorland/definition?id=56804 (last visited on Apr. 24, 2023).

negative ANA. *Id.* An MRI of Petitioner's left shoulder on March 22, 2016, showed a rotator cuff tear as well as tendinitis, bursitis, and a large cystic ganglion. *Id.* at 64-65.

Petitioner also returned to Dr. Philbrick on March 11, 2016. Ex. 4 at 102-04. She complained of continuing tingling and numbness in her hands. *Id.* at 103. Dr. Philbrick noted Petitioner's history of bilateral shoulder impingement, bilateral carpal tunnel syndrome, left side cubital tunnel syndrome, and a recent hospitalization for fainting spells. *Id*. Petitioner's history also included edema in all four extremities and right foot pain that had lasted a few weeks with no traumatic cause. *Id.* Dr. Philbrick noted that Petitioner attributed her orthopedic issues to the flu vaccine she received on December 6, 2015. *Id.* The diagnosis was bilateral carpal tunnel syndrome, right shoulder bursitis, lesion of right ulnar nerve, right foot pain, bilateral hand pain, and osteoarthritis of the carpometacarpal joint of both thumbs. *Id.* at 103-04.

On March 22, 2016, Petitioner underwent an MRI of her left shoulder. Ex. 4 at 62-63. The results were suggestive of "a pinpoint full thickness tear" of the supraspinatus tendon. *Id.* at 63. The results also included biceps tendinosis, mild to moderate acromioclavicular joint degenerative changes, small glenohumeral joint diffusion, trace subacromial-subdeltoid bursitis, and possible focal nondetached tear along the posterior labrum. *Id.*

On March 24, 2016, Petitioner saw her pulmonologist, Daniel Coleman, MD, FCCP, for chronic obstructive pulmonary disease ("COPD"). Ex. 8 at 7-9. He reviewed Petitioner's musculoskeletal symptoms, including right shoulder pain and bilateral wrist and forearm pain, and noted that she "believes that the flu shot was the reason for those symptoms (which seems unlikely . . .)." *Id.* at 7 (ellipsis in original).

On March 31, 2016, Petitioner saw rheumatologist Menachem Kohen, MD. Ex. 7 at 10-11. He noted that Petitioner started to "experience left shoulder discomfort" on the night of her December 6, 2015, flu vaccination, "which after a few days involved also her right shoulder." *Id.* at 10. Dr. Kohen noted that Petitioner had active synovitis in her hands and wrists and bilateral leg edema. *Id.* He diagnosed Petitioner with seropositive RA and started treatment with Plaquenil (hydroxychloroquine) and prednisone. *Id.* at 11. Dr. Kohen noted that "[t]here are descriptions in the literature of new onset inflammatory arthropathies after vaccinations, and since [Petitioner's] symptoms started after the flu vaccination, the vaccination could have been a contributory factor to the onset of her disease." *Id.*

On June 9, 2016, Petitioner saw Dr. Kohen for a follow-up. Ex. 7 at 8-9. He noted that Petitioner experienced "intense hand arthralgias" after discontinuing prednisone and restarted Petitioner on a lower dose. *Id.* Petitioner reported ongoing left shoulder pain which had been temporarily alleviated after a cyst in her left shoulder was drained. *Id.* at 8.

On June 15, 2016, Petitioner saw orthopedist Eric Arvidson, MD, complaining of worsening intermittent left shoulder pain that would sometimes disappear completely. Ex. 4 at 121-22. Dr. Arvidson reviewed Petitioner's spinal x-ray and noted "[c]onsiderable loss of the neural foramen where the C6 nerve root would exit" and "[s]ignificant discogenic disease throughout the spine, however the vertebral body heights are well maintained." *Id.* at 122. Dr. Arvidson thought that Petitioner's symptoms were the result of her cervical pathology, and

pending an MRI, Petitioner's physical therapy was "converted" from shoulder therapy to neck therapy. *Id.* at 122. Petitioner underwent an MRI on July 1, 2016, which showed mild stenosis[8] at C5-6; moderate foraminal narrowing on the right and severe foraminal narrowing on the left; multilevel mild annular disc bulges; and a small central disc protrusion at C3-4. Ex. 4 at 67.

On July 11, 2016, Petitioner returned to Dr. Arvidson complaining of persistent neck pain, especially on the left side. Ex. 4 at 123-24. Dr. Arvidson recommended continuing PT and traction, saying that if invasive treatment was needed, Petitioner would be referred elsewhere. *Id.* at 124.

On August 23, 2016, Petitioner returned to Dr. Kohen for a follow-up for her RA. Ex. 7 at 6-7. Petitioner reported that in general, she felt much better than she had at the beginning of 2016, but that her pain had increased in the prior 24 hours. *Id.* at 6. Dr. Arvidson noted that Petitioner had some relief from her neck and left shoulder discomfort with injections to her cervical spine. *Id.* At a later RA follow-up, Petitioner reported that hand arthralgias were rare and that she was generally feeling better than she had in the past. Ex. 4 at 127.

On November 22, 2016, Petitioner saw Erica Balfour, MS, PAC, at the pain clinic at Holy Family Hospital. Ex. 11 at 110-12. Petitioner's chief complaint was neck pain and she also reported "chronic widespread pain (shoulder, neck, hands) which is associated with [a diagnosis] of 'explosive RA' episode [status post] flu shot in Dec[ember] 2015." *Id.* at 110. Ms. Balfour's assessment was myalgia, cervical radiculopathy, shoulder pain, chronic pain, hand pain, and neuropathy. *Id.* at 111.

On March 4, 2017, Petitioner saw neurologist Marcelo Matiello, MD, for "chronic multifocal pain." Ex. 3 at 2-7. He noted that Petitioner began to experience burning left shoulder pain and then bilateral shoulder pain after her December 2015 influenza vaccination and that the burning pain spread to both of her hands three to four days later. *Id.* at 2. Dr. Matiello suspected sensory polyneuropathy secondary to RA. *Id.* at 6. EMG performed on March 27, 2017, "suggest[ed] the presence of a mild right median sensory neuropathy at the wrist, as may be seen in carpal tunnel syndrome," as well as mild, non-localized right ulnar sensory neuropathy. *Id.* at 10.[9]

On June 27, 2017, Petitioner returned to Dr. Matiello and reported that gabapentin had been helping with her pain. Ex. 3 at 17-22. Dr. Matiello noted that Petitioner's EMG "did not show evidence of sensory polyneuropathy." *Id.* at 21. His impression was a possible small fiber neuropathy and recommended a skin biopsy to confirm. *Id.* A July 5, 2017 skin biopsy was considered diagnostic for a small fiber axonopathy. Ex. 10 at 8.

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[8] Stenosis is "an abnormal narrowing of a duct or canal." DORLAND'S, https://www.dorlandsonline.com /dorland/definition?id=47090 (last visited on Apr. 25, 2023).

[9] In his review of the EMG results, Dr. Matiello also noted that "[v]arious pathological processes have been proposed for vaccine-associated polyneuropathies, with some theories describing immune mediated hypersensitivity to the solvent/adjuvants and/or invasion of nervous system through a prolonged, less virulent infection." Ex. 16 at 5. It is not clear whether Dr. Matiello was aware that Petitioner had received an inactivated, non-adjuvanted component influenza vaccine that is not capable of replication or of causing an infection.

On November 1, 2017, Petitioner saw Dr. Matiello. Ex. 10 at 2-7. His impression was that

> [Petitioner] developed rheumatoid arthritis after a flu vaccination in December 2015. On her neuro exam again today she has diminished pinprick, touch, temperature and vibration, with normal segment position sensation, on both arms and feet. EMG did not show evidence of sensory polyneuropathy. Her skin biopsy shows evidence of small fiber neuropathy. Literature review includes case studies of small fiber neuropathy post flu vaccination. Various pathological processes have been proposed for vaccine associated polyneuropathies, with some theories describing immune-mediated hypersensitivity to the solvents/adjuvants and/or invasion of nervous system through a prolonged, less virulent infection. I recommend that she does not take the flu vaccine this year and continues gabapentin. I will also send her for PT to help with gait and fall precaution. Her symptoms started before she got treatment for her rheumatoid arthritis, so likelihood of her small fiber neuropathy being secondary to methotrexate is small.

Id. at 6.

On March 20, 2018, Petitioner returned to Dr. Kohen for a follow-up for her RA. Ex. 15 at 1-2. Petitioner denied flareup of hands or feet and arthralgias. *Id.* at 1. Petitioner reported mild intermittent hand joint and feet metatarsalgias with morning stiffness, neck pain, and mild bilateral finger paresthesias. *Id.*

On September 4, 2018, Petitioner saw rheumatologist Saba Beg, MD. Ex. 33 at 1322. In a follow-up appointment on November 14, 2019, Dr. Beg described Petitioner's condition as morning stiffness in her hands, no joint pain, and occasional swelling in her hands. *Id.* at 372. Petitioner reported that she was able to do most of the things that she used to do. *Id.*

In her most recent rheumatology appointment with Mazen Nazrallah, MD, Petitioner was reported to be doing well on medication, especially Plaquenil. Ex. 33 at 8-10.

III. Petitioner's Affidavit and Testimony

A. Petitioner's Affidavit

Petitioner signed her affidavit on May 7, 2017. Ex. 2 at 2. In it, she stated that she received the flu vaccine in her left arm on December 6, 2015, and that by that same evening, she was unable to lie on her left side due to intense shoulder pain. *Id.* at 1. Petitioner stated that she visited various doctors, and then was treated by Dr. Kohen, a rheumatologist. *Id.* Petitioner averred that Dr. Kohen told her she had an explosive case of RA most likely triggered by the flu vaccine. *Id.*

B. Petitioner's Testimony

Petitioner testified at the entitlement hearing on August 24, 2021. Tr. at 5-40. Petitioner testified that she had knee replacement surgery in November 2015 and that she received the

allegedly causal flu vaccination on December 6, 2015, at the age of 74. *Id.* at 11-12. Petitioner testified that she received the flu vaccine in her left arm. *Id.* at 13. She stated that she had received flu vaccinations beginning five or six years prior to December 2015 at the recommendation of her pulmonologist. *Id.*

Petitioner testified that she was unable to sleep on her left side the night she received the flu vaccine because of pain in her left shoulder. Tr. at 13. When she woke up on December 7, 2015, the pain had spread to both shoulders and both arms. *Id.* The pain, which Petitioner described as a burning sensation, persisted during the following days. *Id.* at 14. Petitioner went to her pre-scheduled appointment with Dr. Hoerner, her orthopedist, to follow up on her knee replacement a few weeks later. *Id.* at 14-15. She described her shoulder and foot pain, and Dr. Hoerner suggested that the crutches Petitioner was using post-surgery might be causing her shoulder pain.[10] *Id.* at 16. Petitioner was unconvinced by this explanation because she "didn't use the crutches faithfully" while recovering from surgery. *Id.*

Due to Medicare coverage issues, Petitioner had to wait to start shoulder PT until her post-surgical knee PT was complete. Tr. at 17-18. Petitioner underwent PT and occupational therapy ("OT") for her shoulders simultaneously. *Id.* at 18.

Petitioner went on to describe her daily life in the first few months after receiving the flu vaccine. Tr. at 18. She was unable to hold a glass of water without dropping it and could not lift a pot off the stove. *Id.* She had difficulty getting dressed and taking a shower. *Id.* at 18-19. She found it difficult to use the stairs in her home due to fatigue and balance issues. *Id.* at 19.

Petitioner testified that, in February 2016, she was sitting on the couch with her son when suddenly "everything went black, and [she] just fell over." Tr. at 20. Petitioner's son took her to the hospital, where Petitioner received a diagnosis of syncope of unknown origin. *Id.* Her hands were swollen such that she was unable to peel the lids off of paper cups during breakfast the next day. *Id.* at 21; Ex. 35 at 1-2 (photo). Her regular physician, Dr. Gurka, saw her in the hospital and ordered IV Lasix to control the swelling in her hands. *Id.* Petitioner reported that this helped for a while, but that the swelling returned. *Id.*

Petitioner testified that, at Dr. Gurka's recommendation, Petitioner began seeing a rheumatologist, Dr. Kohen, in March 2016. Tr. at 23. She reported she did not feel that her other orthopedist, Dr. Philbrick, had been listening to her about the seriousness of her pain. *Id.* Dr. Philbrick ordered testing that showed a cyst in Petitioner's shoulder. *Id.* at 24. Dr. Kohen also reviewed the results of Petitioner's blood tests and diagnosed her with RA. *Id.* at 25. Dr. Kohen told Petitioner that the flu vaccine could have triggered the explosive onset of her RA, and that he had other patients who had experienced this. *Id.* at 26.

Petitioner testified that Dr. Kohen prescribed prednisone, which did lessen her pain and enable her to sleep better than she had been. Tr. at 26. She reported that "the pain came back with a vengeance" when she stopped taking prednisone. *Id.* at 27. Petitioner began seeing a pain

[10] During her testimony, Petitioner did not recall whether Dr. Hoerner himself or his assistant said this. Tr. at 16.

management specialist on the advice of her orthopedist. *Id.* She began receiving regular cortisone shots. *Id.* at 27-28.

Petitioner testified that, prior to her knee replacement in November 2015, Petitioner had worked as a nurse and victim advocate. Tr. at 10. She was unable to return to work after receiving the flu vaccine because she no longer had the necessary energy or stamina. *Id.* at 28.

Petitioner testified that, in the fall of 2016, she was feeling better except for the burning sensation in her hands. Tr. at 30. Dr. Kohen recommended that she see a neurologist, and Petitioner began seeing Dr. Matiello in early 2017. *Id.* at 30-31. After nerve conduction studies and a skin biopsy, Dr. Matiello diagnosed Petitioner with small axon neuropathy and prescribed gabapentin. *Id.* at 31. In 2017, Petitioner's condition had improved. *Id.* at 32.

Petitioner testified that, the summer before she received the flu vaccine, she had generally felt well. Tr. at 34-35. She was able to get up and leave the house for work between 7:15 and 8:00 a.m. *Id.* at 35. Her work involved attending proceedings in two different courts, completing paperwork, and answering the phone. *Id.* She occasionally went out in the evening after work. *Id.* After the vaccination, she felt she had "hit a wall." *Id.* at 36. She described serious fatigue and difficulty performing everyday tasks. *Id.* She testified that she believes that the flu vaccine she received on December 6, 2015, caused her injury. *Id.* at 37-38.

IV. Expert Opinions and Qualifications

A. Expert Qualifications

1. Petitioner's Expert: Arthur E. Brawer, MD

Dr. Brawer received his medical degree from Boston University in 1972. Ex. 36 ("Brawer CV") at 3. After his internship and residency, he completed a fellowship in arthritis at Boston University Medical Center in 1976. *Id.* Since 1976, he has been in private practice, serving as the Director of Rheumatology and Director of the Arthritis Clinic at Monmouth Medical Center in Long Branch, New Jersey. *Id.* In his practice, Dr. Brawer has seen roughly 25,000 patients, of whom about 10,000 were RA patients. Tr. at 76.

Dr. Brawer is board certified in rheumatology and internal medicine. Brawer CV at 4. He is the author of 41 peer-reviewed publications. *Id.* at 4-10. He has also held teaching positions at Drexel University in Philadelphia and at the Robert Wood Johnson School of Medicine in New Brunswick, New Jersey. *Id.* at 1. I recognized him as an expert in rheumatology and internal medicine. Tr. at 45.

2. Respondent's Expert: Merhdad Matloubian, MD, PhD

Dr. Matloubian received his bachelor's, master's and doctoral degrees (specializing in immunology and virology) from the University of California, Los Angeles. Ex. B at 1, ("Matloubian CV"); First Matloubian Rep. at 1. He completed his residency at the University of

California, San Francisco ("UCSF"), followed by a fellowship in rheumatology, also at UCSF. Matloubian CV at 1. He is board certified in internal medicine and rheumatology. *Id.* at 1-2.

Dr. Matloubian's practice involves a combination of research and patient care. He has served as an associate professor of Medicine at UCSF since 2001. Matloubian CV at 2. In his research, Dr. Matloubian focuses on innate and adaptive immune responses to viral infections, and he has published numerous articles in reputable medical journals on issues in this field. *Id.* at 7–8, 10–14; In addition to teaching and research work, he also serves as associate director of the UCSF Molecular Medicine Consult Service, which is a hospital service involving both clinicians and research scientists, who work together to treat patients with a variety of unusual disorders. Matloubian CV at 3. Additionally, Dr. Matloubian has spent one month per year as an attending physician on the UCSF Inpatient Rheumatology Consult Service since 2001. *Id.* I recognized him as an expert in immunology and rheumatology. Tr. at 117.

B. Pre-Hearing Expert Reports

Prior to the entitlement hearing, Dr. Brawer submitted six expert reports. Exs. 19-23, 27. Dr. Matloubian submitted two expert reports. Exs. A, C.

1. Dr. Brawer: First Expert Report

Dr. Brawer began his first expert report by reviewing Petitioner's medical conditions prior to her December 6, 2015, flu vaccination. Ex. 19 ("First Brawer Rep.") at 1. These included, but were not limited to, COPD, leg edema, calcific tendinitis and rotator cuff damage, and osteoarthritis. *Id.* Dr. Brawer noted that Petitioner began experiencing pain and swelling in her left hand and wrist three days after vaccination which affected her metacarpophalangeal (knuckle) joints and proximal interphalangeal joints in her fingers, "areas completely different from her prior osteoarthritic involvement at the base of the thumb." *Id.* at 1-2. He opined that "the additive polyarthritis subsequent to December 6, 2015 was chronic, intractable, and unremitting on a daily basis." *Id.* at 2. He opined that Petitioner's "clinical picture was highly suggestive of [RA] that had been directly initiated by the influenza vaccination on December 6, 2015." *Id.*

Dr. Brawer criticized Respondent's Rule 4(c) report as having "failed to appreciate the distinction between [Petitioner's] age related osteoarthritic joint involvement from the superimposed systemic inflammatory process of [RA]." First Brawer Rep. at 2. He opined that the mechanism by which the flu vaccine caused Petitioner's RA was "cross reactivity between routinely used vaccine materials and self-antigens in the body." *Id.* He explained that "antigens of infectious agents can cross react with self-antigens present on a variety of body cells, including immunocompetent cells, thereby triggering systemic inflammatory reactions," otherwise known as molecular mimicry. *Id.* at 2-3. In support of this opinion, Dr. Brawer cited medical literature that was never filed. *Id.* Dr. Brawer noted that several medical conditions, including RA, have been linked in the literature with vaccine-induced molecular mimicry. *Id.* at 3.

Dr. Brawer also opined that molecular mimicry is not the only mechanism by which vaccines can trigger autoimmunity, stating that "[a]dverse effects on immunoregulatory cells by vaccines can alter the balance between helper and suppressor T-cells." First Brawer Rep. at 3-4.

He also opined that "[p]olyclonal B-cell activation, a phenomenon routinely present in [RA] patients, can also occur following vaccination." *Id.* at 4.

As to the logical sequence of cause and effect leading to Petitioner's RA, Dr. Brawer opined that Petitioner did not suffer from systemic inflammatory arthritis prior to receiving the flu vaccine. First Brawer Rep. at 4. He further opined that Petitioner's RA "cannot be attributed to any other well defined clinical entity or inflection that could have triggered this condition." *Id.* He added that Petitioner's chronic inflammatory condition began within 24 hours of her flu vaccination "and continued to exist indefinitely." *Id.* He concluded by opining that the there was a temporal relationship between receipt of the flu vaccine and the development of Petitioner's RA. *Id.*

2. Dr. Matloubian: First Expert Report

In his first expert report, Dr. Matloubian began his analysis by stating that he agreed that seropositive RA was the correct diagnosis for Petitioner based on her medical records. Ex. A ("First Matloubian Rep.") at 6. He noted that Petitioner suffered from other non-inflammatory causes of musculoskeletal pain, including osteoarthritis and small fiber neuropathy. *Id.*

Dr. Matloubian provided a detailed description of RA. First Matloubian Rep. at 6-9. He explained that RA is "a systemic inflammatory disease" manifesting in "peripheral arthritis, mainly in the small joints of the hands and feet." *Id.* at 6. Without treatment, RA can cause "deformity and destruction of joints" that are visible on x-ray as "bony erosions." *Id.* Dr. Matloubian explained that RA affects about 1% of Caucasian people and that women are two to three times more likely to develop it, with peak onset occurring between ages 50 and 75. *Id.* at 7.

Dr. Matloubian opined that RA can be difficult to diagnose and that it usually presents with "insidious onset of pain, stiffness, and swelling in multiple joints over the course of weeks to months." First Matloubian Rep. at 7. The American College of Rheumatology and the European League Against Rheumatism developed classification criteria for RA based on four domains: (1) number and site of joints involved; (2) serological abnormalities; (3) elevated ESR and CRP; and (4) symptoms lasting longer than six weeks. *Id.* Dr. Matloubian noted that Petitioner's clinical presentation included shoulder pain, synovitis in the small joints of her hands and her wrists, elevated ESR and CRP, positive rheumatoid factor, and anti-CCP antibodies. *Id.*

Dr. Matloubian opined that the pathogenesis of RA is not well understood, but that genetic and environmental factors are thought to play a role. First Matloubian Rep. at 7. He also opined that, in RA, the breakdown in immune tolerance and development of autoantibodies such as rheumatoid factor and anti-CCP antibodies "precede clinically apparent symptoms by several years." *Id.*

Dr. Matloubian opined that the erosion and synovitis in Petitioner's left knee at the time of her knee replacement in November 2015 "raise[] the likelihood of ongoing asymptomatic RA related synovitis in the petitioner's joints prior to her vaccination, which would be consistent with the current multi-step models of pathogenesis of RA." First Matloubian Rep. at 8. Dr. Matloubian opined that medical literature supports the idea that the RA disease course is divisible into multiple

phases. *Id.* One such model proposes six phases: (1) genetic risk factors; (2) environmental risk factors (e.g., smoking, antibiotics); (3) systemic autoimmunity; (4) clinical symptoms; (5) unclassified arthritis; and (6) RA. *Id.* (citing van Steenbergen, et al., *The Preclinical Phase of Rheumatoid Arthritis: What is Acknowledged and What Needs to Be Assessed?*, 65(9) ARTHRITIS & RHEUMATISM 2219-32 (2013) (filed as Ex. A, Tab 11)). Dr. Matloubian opined that factors such as infections, toxins, drugs, and radiation may impact this progression in a particular patient, but that the long lag time between development of autoantibodies and clinical disease makes causation very difficult to establish. *Id.* at 9. Dr. Matloubian also opined that the apparent complexity of the pathogenesis of RA makes "simplistic explanations, such as molecular mimicry," less likely. *Id.*

Dr. Matloubian next turned to Petitioner's case. First Matloubian Rep. at 9. He criticized Dr. Brawer's expert report, opining that Dr. Brawer ignored significant evidence in the literature in which researchers have found no evidence of a causal link between vaccines and RA. *Id.* at 9-10 (citing Ray, et al., *Risk of rheumatoid arthritis following vaccination with tetanus, influenza and hepatitis B vaccines among persons 15-59 years of age*, 29 VACCINE 6592-97 (2011) (filed as Ex. A, Tab 17) ("Ray"); Fomin, et al., *Vaccination against influenza in rheumatoid arthritis: the effect of disease modifying drugs, including TNFα blockers*, 65 ANNALS OF RHEUMATIC DISEASES 191-94 (2006) (filed as Ex. A, Tab 18) ("Fomin"); Bengtsson, et al., *Common vaccinations among adults do not increase the risk of developing rheumatoid arthritis: results from the Swedish EIRA study*, 69 ANNALS OF RHEUMATIC DISEASES 1831-33 (2010) (filed as Ex. A, Tab 19) ("Bengtsson"). He also disagreed with Dr. Brawer's reliance on case reports because they lack control groups and only show "temporal associations of two events in a few individuals." *Id.* at 10. Dr. Matloubian also pointed out that "the American College of Rheumatology recommends influenza immunization of individuals with autoimmune diseases, including RA," and that "despite millions of people being vaccinated each year with influenza virus, reports of temporally related onset of arthritis is quite rare." *Id.* at 11-12.

Dr. Matloubian disagreed with Dr. Brawer's theory of molecular mimicry as the mechanism by which the flu vaccine can cause RA. First Matloubian Rep. at 12. He opined that, with the exception of streptococcal bacterial infection causing rheumatic fever, molecular mimicry "has rarely been persuasively demonstrated as the cause of autoimmunity in humans." *Id.* He further opined that in order for molecular mimicry to be relevant here, the natural flu infection should also cause RA in some patients, but it does not. *Id.* He criticized Dr. Brawer's bystander activation hypothesis, opining that because natural flu infection elicits a stronger immune response than the flu vaccine does, we would expect to see RA caused by flu infections more often than by the vaccine. *Id.*

Dr. Matloubian next questioned Dr. Brawer's reliance on an unfiled article by Kanduc, et al. to support his claims about peptide sequence homology between the flu vaccine and self-antigens in the body, calling a simple sequence homology "meaningless." First Matloubian Rep. at 12 (citing First Brawer Rep. at 3). He cited medical literature stating that "'[m]any such homologies exist, and the vast majority of these are not associated with biologically relevant autoimmune phenomena or actual human disease.'" *Id.* at 12-13 (citing INSTITUTE OF MEDICINE, *Adverse Effects of Vaccines: Evidence and Causality* (2012) (filed as Ex. A, Tab 25)). He opined that, in any case, there is strong indication in the medical literature that there is no molecular mimicry between the flu virus and self-antigens associated with RA. *Id.* at 13.

Dr. Matloubian also disagreed with Dr. Brawer's opinion that the flu vaccine caused Petitioner's RA because symptom onset was too close in time to her flu vaccination. First Matloubian Rep. at 13. He noted that "the autoimmune process that leads to development of this disease begins years before the disease becomes clinically apparent." *Id.* Therefore, he opined that "it would be virtually impossible for an immune response to be initiated and cause symptoms within 24 hours and lead to all of her symptoms within 3-4 days as alleged by Dr. Brawer." *Id.* He opined that the B and T cell response needed to cause inflammation would have taken seven to 14 days to reach its peak, plus additional time for those cells to travel to the affected joints. *Id.*

Dr. Matloubian stressed that the cause of RA in a particular case, including Petitioner's, is not ascertainable. First Matloubian Rep. at 13. He pointed out that Dr. Brawer is the author of a paper finding a link between traumatic injury and development of RA. *Id.* (citing Brawer & Goel, *The onset of rheumatoid arthritis following trauma*, 8 OPEN ACCESS RHEUMATOLOGY: RES. & REVS. 77-80 (2016) (filed as Ex. A, Tab 29) ("Brawer & Goel")). Dr. Matloubian opined that Dr. Brawer's own research supports the contention that Petitioner's knee replacement surgery in November 2015 was "an example of direct joint trauma." *Id.* at 14. He posited that "[a]n invasive procedure such as joint replacement provides an ideal opportunity for the joint related self-antigens to be released into the blood stream and initiate an autoimmune response." *Id.* He also argued that the timing of onset after surgery (roughly one month) is consistent with the findings in Dr. Brawer's article. *Id.*

Finally, Dr. Matloubian disagreed with Dr. Brawer's reliance on Petitioner's symptoms having begun on the day of her vaccination. First Matloubian Rep. at 14. He opined that this could have been a coincidence, citing medical literature that calculated the likelihood of coincidental RA onset after vaccination. *Id.* (citing Ahmed, et al., *Assessing the safety of adjuvanted vaccines*, 3(93) SCI. TRANSLATIONAL MED. 1-10 (2011) (filed as Ex. A, Tab 30) ("Ahmed"). The authors found that, based on the statistical likelihood of developing RA and the number of vaccine doses administered, we have a 90% chance of seeing one case of RA onset coinciding with vaccination for every 10,000 vaccine doses administered. Ahmed at 7. Dr. Matloubian opined that, "[t]aking into account that 150 million people are annually immunized with influenza in the U.S., we would expect then that 15,000 individuals would develop RA after such vaccination due to coincidence alone." *Id.* He concluded that, a woman's lifetime risk of developing RA being one in 28, Petitioner's RA was more likely that not unrelated to her flu vaccination. *Id.*

3. Dr. Brawer: Second Expert Report

In his second expert report, Dr. Brawer criticized Dr. Matloubian as being "first and foremost a researcher" with limited clinical experience. Ex. 20 ("Second Brawer Rep.") at 1. In fact, he spent a significant portion of the report levelling personal attacks against Dr. Matloubian. Dr. Brawer wrote that Dr. Matloubian had "a cookie cutter one size fits all approach to [RA] that is untempered by clinical reality." *Id.* Later in his report, he referred to Dr. Matloubian's analysis as "feeble", described his opinions as the "epidemiologic ramblings of a research scientist", and

stated that the "usefulness and validity" of his expert report was "inversely related to its length." *Id.* at 2-3.[11]

Dr. Brawer went on to opine that RA is a complex disease with "numerous predisposing factors other than genetic predisposition and HLA susceptibility," including, but not limited to, physical injury, infection, smoking, hormonal imbalance, and vaccinations. Second Brawer Rep. at 1. He opined that the initial inflammatory events in the early days and weeks of RA in patients whose disease is triggered by one of these predisposing factors is different from those in a case of "classical spontaneous" development of RA. *Id.* He added that laboratory testing can be confusing or misleading in cases where RA develops due to one of the above triggers because the typical blood markers may be absent even when a patient meets all of the diagnostic criteria for RA. *Id.*

4. Dr. Brawer: Third, Fourth, and Fifth Expert Reports

Petitioner next filed three supplemental expert reports from Dr. Brawer on the same day.

Dr. Brawer began his third expert report by opining that the "immunologic landscape in [RA] encompasses an extraordinary collection of complex phenomena." Ex. 21 ("Third Brawer Rep.") at 1. Dr. Brawer described research into the "spontaneous, chronological pre-clinical immunologic events preceding the onset of [RA] symptoms and signs," such as those listed in his second expert report. *Id.* He opined that such immunologic triggers for RA are relevant in about 25% of cases. *Id.* He opined that these triggers initiate "cascades of inflammation" that lead to the

[11] Dr. Brawer's use of personal insults and disparaging language against Dr. Matloubian was such that I twice addressed the issue with Petitioner's counsel during status conferences. ECF Nos. 43, 53. I informed counsel that such conduct is unhelpful and detracts from Dr. Brawer's medical opinion. ECF No. 53. I further note that my colleagues have previously remarked upon Dr. Brawer's use of language *identical* to that employed in Petitioner's case. *McDonald v. Sec'y of Health & Hum. Servs.*, No. 15-612V, 2023 WL 2387844, at *6 (Fed. Cl. Spec. Mstr. Mar. 7, 2023) (noting that Dr. Brawer engaged in unnecessary personal criticism of Respondent's expert when he stated that Dr. Wallace's expert report "manifests a 'cookie cutter' view of neurological fatiguing syndromes … untampered [sic] by clinical reality."); *Whelan v. Sec'y of Health & Hum. Servs.*, No. 16-1174V, 2019 WL 1061473, at *4 fn. 10 (Fed. Cl. Spec. Mstr. Jan. 28, 2019) (stating "Dr. Brawer also dedicates a sizable portion of his supplemental report to criticizing Dr. Matloubian's report, largely by way of ad hominem attacks on Dr. Matloubian himself,…characterizing Dr. Matloubian as … having 'a cookie-cutter, one-size fits all approach to inflammatory systemic connective tissue diseases that is untampered [sic] by clinical reality,'…and asserting that 'the usefulness and validity of Dr. Matloubian's report of November 28, 2017 is inversely related to its length')"); *Braun v. Sec'y of Health & Hum. Servs.*, No. 16-1098V, 2018 WL 2375751, at *15 (Fed. Cl. Spec. Mstr. Apr. 24, 2018) (noting Dr. Brawer's remark that "'Dr. Matloubian has a cookie cutter, one size fits all approach to [systemic lupus erythematosus] that is untampered [sic] by clinical reality.'"). It is, of course, well within the purview of an expert witness to express disagreement with the opinion of another expert witness. However, I find that Dr. Brawer's continued disparaging remarks about Dr. Matloubian's opinion, experience, and character went beyond professional disagreement and were both unnecessary and unhelpful.

development of RA. *Id.* He stated that traditional, "'classical'" models of RA do not take this into account. *Id.*

Dr. Brawer went on to opine that the theories discussed in his first expert report may not be the exclusive cause of RA. Third Brawer Rep. at 1. Rather, they "may eventually wind up being secondary amplification loops that confer chronicity to [RA] once it has been acutely triggered" by vaccine-induced inflammatory cascades. *Id.* He opined that assigning a precise timeline to vaccine-induced RA onset is difficult, stating that "chronological parameters are not compatible with the broad spectrum of medical realities." *Id.* at 1-2.

Dr. Brawer began his fourth expert report by stating that "[t]he discrepancies and confusion in this case can essentially be distilled down to one simple fact: immunological disturbances in the human body are not synonymous with inflammatory disturbances in the human body." Ex. 22 ("Fourth Brawer Rep.") at 1. He added that immune dysregulation can cause chronic inflammation, but that it does not always, and that, likewise, acute inflammation can cause local immunologic disturbance that then disseminates to other parts of the body. *Id.*

Dr. Brawer reiterated his list of triggers that can initiate systemic inflammatory processes. Fourth Brawer Rep. at 1. He opined that each trigger can initiate acute inflammation that can lead to "the local appearance of immunocompetent cells," which in turn can lead to widespread inflammatory conditions such as RA. *Id.* He noted that, while diagnosis of RA requires at least six weeks of continuous polyarthritis, in about 10 percent of cases of idiopathic RA, onset begins in a single joint and does not spread to other joints for five years. *Id.* He opined that this fact "implies that diverse disjointed mechanisms of disease progression are operative." *Id.*

Dr. Brawer discussed the example of mono- or polyarthritis caused by viral infection. Fourth Brawer Rep. at 1-2. He explained that infection-associated arthritis can persist after the resolution of other symptoms and eventually evolve into RA. *Id.* He stressed the heterogeneity of laboratory findings in such cases, especially the white cell counts in synovial fluid, and argued that this is evidence that "multiple mechanisms of disease causation are operative." *Id.* at 2.

Dr. Brawer stated that recent medical literature supports an increased risk of developing RA and systemic lupus erythematosus "following severe emotional upset." Fourth Brawer Rep. at 2. He noted that there is evidence that severe childhood trauma (e.g., the loss of a parent) is associated with increased risk of developing RA as an adult. *Id.* He also described cases he has seen in his clinical practice wherein severe temperature exposure triggers acute onset of RA. *Id.*

Dr. Brawer concluded by reiterating his opinion that the timeline of onset of RA after a triggering event is highly variable, from 24 hours to three weeks. Fourth Brawer Rep. at 2. He also reiterated his opinion that theories pertaining to idiopathic RA do not pertain to cases of RA triggered by the events he has described. *Id.*

In his fifth expert report, Dr. Brawer opined that Petitioner's flu vaccination "triggered an immediate and brisk inflammatory response," the persistence of which "implies that immunocompetent cells had joined the reaction." Ex. 23 ("Fifth Brawer Rep.") at 1. He further opined that Petitioner's immunologic response spread to other parts of her body by means of

"cellular proliferation and migration," resulting in autoimmunity and RA. *Id.* He argued that vaccine-induced disease mechanisms "become accompanied by multiple slowly escalating amplification loops comprising other adverse immunologic responses." *Id.*

Dr. Brawer opined that it is likely that multiple mechanisms of vaccine-induced disease operate at the same time, but that their effects are not necessary felt simultaneously. Fifth Brawer Rep. at 1. He reiterated his opinion that an onset window of 24 hours to several weeks was plausible. *Id.*

5. Dr. Matloubian: Second Expert Report

In his second expert report, Dr. Matloubian responded to Dr. Brawer's second, third, fourth, and fifth expert reports. Ex. C ("Second Matloubian Rep.") at 1. Dr. Matloubian opined that Dr. Brawer's theory of causation in this case "is entirely based on a temporal relationship between two events: vaccination and development of disease." *Id.* He criticized Dr. Brawer's reliance on case reports and anecdotes from his clinical practice and his lack of consideration for peer-reviewed literature. *Id.*

Dr. Matloubian reiterated his opinion that the timing of symptom onset in Petitioner's case cuts against vaccine causation because "RA begins years before the affected individual becomes symptomatic." Second Matloubian Rep. at 2.

Dr. Matloubian disagreed with Dr. Brawer's list of environmental triggers for RA because some of them "have not been substantiated by careful and controlled research, whose goal is to distinguish coincidence from causation." Second Matloubian Rep. at 2. He opined that evidence in the literature that vaccines can trigger RA is based on case reports only and that only female sex and a history of smoking have been consistently shown to raise the risk of developing RA. *Id.* He also opined that environmental factors that influence the transition from pre-clinical to clinical RA would not act within 24 hours as Dr. Brawer contends. *Id.*

Dr. Matloubian also explained in greater detail his critique of Dr. Brawer's reliance on case reports. Second Matloubian Rep. at 3. He reiterated his opinion that coincidence cannot be ruled out without a control group. *Id.* He also opined that a serious problem with case reports is that the author does not discuss the entire medical record, but rather the selections from it that he or she deems relevant. *Id.* at 4. The issue with this, Dr. Matloubian argues, is that there may be parts of the medical record that are arguably relevant to causation that are left out of the case report. *Id.* As an example, Dr. Matloubian stated that he served as Respondent's expert in one of the cases in the article by Brawer & Koyoda that was litigated in the Vaccine Program, and thus had access to the entire medical record. *Id.* He took issue with the decision in Brawer & Koyoda not to discuss the patient's case of GBS four months after vaccination as being relevant to their conclusion that her vaccination may have caused her to develop lupus erythematosus. *Id.* (citing Brawer & Koyoda, *The onset of rheumatoid arthritis and systemic lupus erythematosus following influenza vaccination: Report of three cases*, 4:3 CLIN. MICROBIOL. & INFECTIOUS DISEASE 1-3 (2019) (filed as Ex. 25) ("Brawer & Koyoda")). Dr. Matloubian opined that the increased muscle enzymes that Dr. Brawer attributed to her lupus may actually have been related to her GBS, and used this case

to illustrate his opinion that case reports are not good evidence of causal relationships because parts of the medical record may be left out. *Id.*

Dr. Matloubian concluded by distinguishing his analysis from Dr. Brawer's, stating that his opinion was based "not on [his] personal experience, but on what the experts have published in the literature based on their analysis of carefully done controlled studies." Second Matloubian Rep. at 4.

6. Dr. Brawer: Sixth Expert Report

Dr. Brawer began his sixth expert report by criticizing Dr. Matloubian for having "once again redundantly regurgitated the mechanisms of [RA] beginning spontaneously." Ex. 27 ("Sixth Brawer Rep.") at 1. He reiterated his opinion that the mechanisms of idiopathic RA differ from those in cases of vaccine-induced RA. *Id.* Dr. Brawer also took issue with Dr. Matloubian's critique of Dr. Brawer's recent publication. *Id.* (citing Brawer & Koyoda). He opined that Dr. Matloubian "obviously prefers that one unilaterally and compartmentally evaluate any medical case solely by perusal of statements in a single hospital chart" and that Dr. Matloubian's remarks on the case in Brawer & Koyoda "should, without reservation, be completely disregarded." *Id.* at 2. He referred to Dr. Matloubian's remarks as "callous" and suggested that they "are more likely to adversely reflect on his own flippant integrity and truncated clinical experience." *Id.*

C. Expert Testimony

1. Dr. Brawer

At the entitlement hearing, Dr. Brawer stated that, prior to her December 6, 2015, flu vaccination, Petitioner suffered from COPD, atrial fibrillation, leg edema, allergic rhinitis, gastroesophageal reflux, penicillin allergy, hemorrhoids, calcific tendinitis and rotator cuff damage in her shoulders, and degenerative joint disease, also known as osteoarthritis, in her knees, spine, and some small joints in her hands. Tr. at 46-47. Dr. Brawer explained that osteoarthritis is the kind of arthritis that frequently happens in old age. *Id.* at 47. He explained that osteoarthritis has a typical distribution in the body and that it "differs significantly from inflammatory conditions such as [RA]." *Id.*

Dr. Brawer testified that he had reviewed the lab work ordered by Dr. Hoerner and explained that the ESR "is essentially a blood test for inflammation." Tr. at 48. He opined that a normal result for a person of Petitioner's age would be 30 or less. *Id.* He noted that Petitioner's ESR was normal just before her knee replacement surgery in November 2015 while she was already suffering from osteoarthritis. *Id.* at 48-49. Dr. Brawer went on to explain that the rheumatoid factor is a test "that is usually positive in about 80% of patients with [RA]," and that it is not typically tested unless RA is suspected. *Id.* at 50. He opined that Petitioner's rheumatoid factor after vaccination was "markedly positive." *Id.* He opined that osteoarthritis does not evolve into RA because osteoarthritis is not a systemic inflammatory autoimmune disease. *Id.* at 51.

Dr. Brawer testified that there is evidence in the medical literature to suggest that RA may be a syndrome rather than a disease, and that chronic inflammation can lead to systemic

autoimmune diseases such as RA. Tr. at 52. He referred to a study conducted in Scandinavia in the 1970's that examined cases of RA following skiing injuries. *Id.* at 53. The authors found that the rates of positive ANA among subjects was 10 to 12 percent within one week of injury, 14 percent within two weeks, and 20 percent within three weeks. *Id.* (citing Julkunen, et al., *Severe trauma as an etiologic factor in rheumatoid arthritis*, 3 SCANDINAVIAN J. RHEUMATOLOGY 97-102 (1974) (filed as Ex. 42) ("Julkunen")). Dr. Brawer testified that the findings of this study led to further research into "how physical injuries could initiate chronic inflammation at the site of the injuries and then lead to the spread of that inflammation to multiple other joints…and eventually morph into [RA]." Tr. at 55. This research suggests that chronic inflammation, regardless of how it is initiated, if unchecked, can trigger a systemic immunologic reaction that can lead to chronic disease, including RA. *Id.* at 55-56.

Dr. Brawer testified that it is not possible for a total knee replacement to trigger RA because the procedure involves the removal of the entire synovium, which is the source of inflammation and joint destruction in RA. Tr. at 56. Accordingly, he opined that Petitioner's knee replacement surgery was not relevant to the cause of her RA. *Id.* at 57.

Dr. Brawer testified that, in Petitioner's case, three questions must be asked: (1) what condition Petitioner has; (2) how Petitioner got it; and (3) why, or by what mechanism, Petitioner got it. Tr. at 57. He added that he finds theories of molecular mimicry problematic because they do not explain why a variety of vaccines can cause the same condition, or why one vaccine can cause a variety of conditions. *Id.* at 58.

Dr. Brawer testified that at least half a dozen mechanisms can participate in the production of vaccine-induced autoimmunity. Tr. at 59. He stated that "multiple mechanisms may be triggered on day one of the vaccination, [but] they are not necessarily all clinically relevant on day one of the vaccination." *Id.* He opined that what is required is "a perfect storm," which is to say that "half a dozen things need to come together to produce vaccine toxicity, and molecular mimicry is only one part of that." *Id.* at 60.

Dr. Brawer explained his theory of causation as follows:

> [I]f you have localized inflammation set up in a certain area from the vaccine and it doesn't quiet down, that inflammation is capable of recruiting immunocompetent cells. That inflammation is capable of then having that inflammation travel to distant areas by various mechanisms…if it goes on for six weeks or longer in multiple joints, then you have to decide whether indeed the [RA] was indeed triggered by the vaccination.

Tr. at 60.

Dr. Brawer noted that the vast majority of people tolerate vaccines well and opined that only in cases of "the perfect storm" will a vaccine cause autoimmune disease. Tr. at 60. He opined that "the perfect storm" requires involvement of regulatory T cells, the cells responsible for regulating and shutting down the immune response that occurs upon vaccination. *Id.* at 61. Dr. Brawer posited that the failure of regulatory T cells to shut down the immune response is partly to

blame for the overactive immune response leading to autoimmunity. *Id.* Dr. Brawer went on to opine that channelopathies[12] are relevant to regulatory T cells, as well as to other immunocompetent cells. *Id.* at 62. Dr. Brawer explained that, of the roughly 400 known channelopathies, over 300 do not have any clinical consequence without a triggering event (e.g., a febrile seizure). *Id.*

Dr. Brawer opined that several factors are required to create "the perfect storm" and lead to autoimmunity, including "regulatory T cell dysfunction, chemical toxicity, channelopathies, mitochondrial dysfunction, and what we call DAMPs, or damage-associated pathogens, molecular pathogens." Tr. at 63. He went on to opine that this heterogeneity may explain why one vaccine can cause several different autoimmune problems and why the same autoimmune problem can be caused by several different vaccines, as well as the diversity in timing of disease onset. *Id.* at 64.

Dr. Brawer testified that he cannot explain why a patient experiences "the perfect storm" and autoimmunity upon receiving a vaccine when the same patient received previous vaccines without incident. Tr. at 64. He added that he has seen this happen in his practice. *Id.*

Dr. Brawer opined that Petitioner had chronic inflammation at the vaccination site that spread from one shoulder to the other, and then to her wrists and hands. Tr. at 65-66. He noted that these are not the joints normally affected by osteoarthritis. *Id.* at 66. He posited that Petitioner's condition was "an additive polyarthritis that then [became] chronic." *Id.*

Dr. Brawer next addressed Petitioner's testimony that she suffered from neuropathy. Tr. at 67. He opined that Petitioner had "several types of neuropathies. I think she had some entrapment phenomenon at her wrists that produced carpal tunnel syndrome." *Id.* He explained that swelling in the wrists can compress the nerves that lead to the fingers, causing pins-and-needles sensations and pain in the fingers and hands. *Id.* He testified that neuropathies are among the extra-articular manifestations of RA, along with "rheumatoid nodules…Sjogren's syndrome, dryness in the eyes." *Id.* at 68.

Dr. Brawer testified that RA is a complex disease with "numerous predisposing factors other than genetic predisposition and HLA susceptibility." Tr. at 69. These include, but are not limited to, physical injuries, infections, severe emotional upset, exposure to chemicals such as pesticides, smoking, hypoxia, hormonal imbalance, prolonged exposure to unusual temperature changes, and vaccinations. *Id.* at 69-70. Dr. Brawer opined that these triggers "actually account for the vast majority of cases as opposed to the traditional concepts…that this is an immunologic

[12] Dr. Brawer alluded to his own research on channelopathies, which explains that "[s]odium, potassium, and other ions routinely fluctuate in and out of cells through pores (channels) in cell membranes. Channelopathies are diseases caused by disturbed function of ion channel components and/or the proteins that regulate them. These diseases are either congenital (i.e., from a mutation in one or more genes encoding the proteins) or acquired. Examples of the latter can occur from autoimmune attack on ion channel proteins, ligand anomalies, or from chemical toxicity." Arthur Brawer, *Vaccination Induced Diseases and their Relationship to Neurologic Fatiguing Syndromes, Channelopathies, Breast Implant Illness, and Autoimmunity via Molecular Mimicry*, 4 INT'L J. VACCINES & IMMUNIZATION 1-5, at 2 (2020) (filed as Ex. 31) ("Brawer").

problem that begins decades or several months or several years before the actual joint inflammation itself occurs." *Id.* at 70. He opined that RA "is getting more perplexing, not less perplexing." *Id.*

Dr. Brawer gave three reasons for his opinion that the flu vaccine caused Petitioner's RA. Tr. at 71. First, Petitioner did not have RA prior to vaccination on December 6, 2015. *Id.* Second, "the chronological sequence of events is very classical for vaccine-induced toxicity producing an autoimmune problem." *Id.* Finally, he opined that, but for the flu vaccine, Petitioner likely would not be suffering from RA. *Id.*

Dr. Brawer testified that he bases his theories in this case on his 46 years as a clinician. Tr. at 72. He acknowledged that his theories still require verification or refutation in a research setting. *Id.* He reiterated his opinion that vaccine-induced toxicity is the result of many factors and opined that molecular mimicry alone is not enough. *Id.* at 72-73.

Dr. Brawer responded to Dr. Matloubian's reliance on medical literature in his expert reports, opining that "you can't force fit the patients into the research. The researchers have to explain what we see at the bedside." Tr. at 75. Dr. Brawer opined that the onset of Petitioner's RA occurred very soon after she received the vaccine because of the inflammatory response, which precedes the immunologic response. *Id.* at 77.

On cross examination, Dr. Brawer testified that, while he is not certified to practice alternative medicine, he has written a book on the subject and "do[es] apply alternative medicine disciplines" to some patients. *Id.* at 81.

Dr. Brawer testified that, in one of his articles, he discusses three cases of post-vaccination injury, each of which was litigated in the Vaccine Program. Tr. at 82-83 (citing Brawer & Koyoda). He conceded that he served as petitioner's expert witness in each of the three cases, but he opined that there was no conflict of interest in doing so because he evaluated each case on its merits. *Id.* at 86. Dr. Brawer agreed with the statement that temporal association between vaccination and autoimmunity is not enough to establish causation. *Id.* at 89.

Dr. Brawer testified that, in his practice, he has known infections to be causally related to seropositive RA. Tr. at 89. He added that he has seen patients present with a viral infection and abnormal liver function in whom the arthritis persists after the other symptoms resolve. *Id.* at 90-91. He declined to state that *any* vaccination can cause RA, but opined that both the hepatitis B and measles, mumps, and rubella ("MMR") vaccines can. *Id.* at 91, 93.

Dr. Brawer opined that it is highly probable that, in Petitioner's case, components of the flu vaccine played a role in influencing epigenetics, leading to Petitioner's injury. Tr. at 98. He explained that vaccine additives can alter gene expression (i.e., "genes may turn off that should be turned on, or genes that turn on that should be turned off."). *Id.* at 97-98.

Dr. Brawer opined that Petitioner's initial inflammation was in her left shoulder. Tr. at 99. He added that this was in the context of her chronic illness but was only diagnosable as RA after it had persisted for six weeks. *Id.* at 99-100. Dr. Brawer maintained that it is clear that Petitioner's RA began within 24 hours of receiving the flu vaccine. *Id.* at 102-03.

I asked Dr. Brawer to succinctly summarize his theory of causation under prong one of *Althen*. Tr. at 102. He replied that "there are essentially roughly half a dozen different elements participating in the production of vaccine toxicity that can then trigger a systemic autoimmune condition." *Id.* at 103. He added that "these entities may not necessarily all be clinically relevant on day one or day two of the vaccination process." *Id.* He opined that "molecular mimicry has some role in this, but it certainly cannot possibly exist by itself, and probably doesn't become clinically relevant until three or four weeks after the initial vaccination." *Id.* He opined that "chemicals in the vaccine are capable of initiating acute inflammation," and that "in the presence of certain chemicals, these ion channels become dysfunctional," leading to channelopathy. *Id.* at 104. He continued, stating that "there are ion channels in immunocompetent cells, including regulatory T cells and including macrophages and dendritic cells and polymorphoneuclear leukocytes." *Id.* He opined that channel dysfunction of immunocompetent cells is "part of this augmentation-amplification loop causing dysfunction that can become self-perpetuating." *Id.* He added that dysfunctional mitochondria within cells "are capable of initiating both autoinflammatory and autoimmune processes." *Id.* He emphasized that the "incredible diversity and heterogeneity [of] vaccine toxicity" is evidence that [t]here has to be more than just one component." *Id.* at 106.

Dr. Brawer concluded by opining that a flu infection can cause RA, but that it is "very rare." Tr. at 107.

On redirect examination, Dr. Brawer testified that osteoarthritis causes inflammation and synovitis in the joints, but that these processes are different from the inflammation and synovitis caused by RA. Tr. at 186. He opined that, while the pathology report on Petitioner's knee at the time of her replacement surgery found synovitis, bone resorption, and erosion, "these are common findings in end-stage osteoarthritis" and do not indicate that Petitioner had RA. *Id.* Dr. Brawer disagreed with Dr. Matloubian, saying that "it's simply preposterous to assume that [Petitioner] had [RA] in her knee superimposed on her osteoarthritis just because a pathologist described synovitis and bone erosion and loss of cartilage." *Id.* at 187.

Dr. Brawer opined that RA most often occurs in women younger than Petitioner (i.e., between the ages of 30 and 50). Tr. at 187. He also criticized Dr. Matloubian's testimony that Petitioner had nonerosive RA because an x-ray would be needed to make this determination. *Id.* at 188. He opined that this claim was inconsistent with Dr. Matloubian's other contention that Petitioner's knee pathology showed erosions and bone loss. *Id.*

Dr. Brawer testified that patients with osteoarthritis frequently develop calcium deposits in the synovium and surrounding tissues. Tr. at 197. He opined that these deposits can cause the pathological features of osteoarthritis to take on the appearance of RA, and that accompanying synovitis can resemble RA inflammation because inflammatory and immunocompetent cells are present in the synovium and bone erosion occurs. *Id.* He reiterated his opinion that Petitioner did not have RA prior to receiving the flu vaccine on December 6, 2015. *Id.* at 198.

2. Dr. Matloubian

Dr. Matloubian also testified at the entitlement hearing. Tr. at 110-85. He began by explaining that RA is "a chronic autoimmune inflammatory arthritis" affecting the joints, as well as other organs. Tr. at 117-18. He testified that RA affects about 1% of the Caucasian population and is about three times more common in women than in men. *Id.* at 118. He added that peak onset is during the ages of 50 to 75, but onset can occur at any age. *Id.* Dr. Matloubian explained that in RA, B lymphocytes and T cells begin to attack parts of the body, causing chronic inflammation and damage. *Id.* at 118-19. There are two types: seropositive RA, which is associated with anti-CCP[13] positivity; and seronegative RA, in which the patient exhibits clinical symptoms of RA, but is negative for anti-CCP antibodies. *Id.*

Dr. Matloubian opined that HLA, or human leukocyte antigen, alleles are thought to play a role in RA. Tr. at 120, 122.

Dr. Matloubian testified that diagnosis of RA begins with a clinical diagnosis of inflammatory arthritis consistent with RA, which involves a physical exam and taking of the patient's medical history, and a finding of active joint inflammation or synovitis. Tr. at 120-21. The clinical diagnosis is then confirmed with x-rays and blood tests. *Id.* at 121. A positive test for anti-CCP antibodies will lead to a diagnosis of seropositive RA. *Id.* Dr. Matloubian reiterated his opinion that Petitioner has seropositive nonerosive RA. *Id.* at 122.

Dr. Matloubian opined that the pre-clinical phase of Petitioner's RA began prior to her December 6, 2015, flu vaccination. Tr. at 122. He also opined that the pre-clinical phase of RA can last for many years, and on average lasts three to five years. *Id.* He cited the synovitis and erosion in Petitioner's left knee at the time of her knee replacement in November 2015 as evidence that she already had RA at that time. *Id.* at 123. Dr. Matloubian explained that synovitis is the proliferation of the synovium, the layer that lines the joint capsule. *Id.* at 123. Ordinarily, the synovium is only one cell thick, and synovitis results in a mass of cells rather than a thin layer. *Id.*

Dr. Matloubian explained that osteoarthritis is different from RA in that it is a degenerative bone disease resulting from normal wear and tear on joints as the body ages. Tr. at 124. He opined that osteoarthritis is characterized by loss of cartilage and consequent growing of additional bone material, and thus is not consistent with erosion. *Id.* He opined that synovitis accompanied by erosion is not typically associated with osteoarthritis either. *Id.* He explained that erosion is the invasion of bone by the proliferating synovial cells. *Id.* He cited medical literature supporting the contention that synovitis can be present in a joint before the patient feels symptoms of RA. *Id.* at 125-26 (citing Kraan, et al., *Asymptomatic synovitis precedes clinically manifest arthritis*, 41(8) ARTHRITIS & RHEUMATISM 1481-88 (1998) (filed as Ex. A, Tab 9) ("Kraan") (reporting that biopsy showed evidence of synovitis in asymptomatic joints in RA patients)). Dr. Matloubian opined that it is more likely than not that Petitioner had anti-CCP antibodies and positive rheumatoid factor prior to vaccination based on the predominant view in the field of seropositive RA. *Id.* at 128-29.

[13] Dr. Matloubian testified that "anti-CCP" refers to antibodies that attack cyclic citrullinated peptides.

Dr. Matloubian expressed the opinion that it is more likely than not that the flu vaccine played no role in her RA. Tr. at 129. He noted that Petitioner is female and a former smoker, both of which are risk factors for developing RA. *Id.* at 130. He also noted that her disease onset occurred during the typical age range. *Id.*

Dr. Matloubian opined that there is no association between the flu vaccine and development of RA. Tr. at 130. In support of this opinion, he noted that the current guidance in the medical community is to recommend annual flu vaccination to patients with RA. *Id.* He opined that the medical literature indicates that RA patients respond to the flu vaccine itself, but that it does not lead to disease flares in RA patients. *Id.* He denied that there is any evidence of molecular mimicry between components of the flu vaccine and antigens known to be involved in RA development. *Id.* at 131.

Dr. Matloubian next elaborated on his opinion that a history of smoking increases the risk of developing RA. Tr. at 131. He cited medical literature positing a link between smoking and citrullinated peptides that bind to HLAs and elevate the risk of RA. *Id.* at 131-32 (citing Malmström, et al., *The immunopathogenesis of seropositive rheumatoid arthritis: from triggering to targeting*, NATURE REVS.: IMMUNOLOGY 1-16 (2016) (filed as Ex. A, Tab 4)). He noted that Petitioner had smoked roughly half a pack of cigarettes per day for four years prior to 1979. *Id.* at 132. He declined to say for certain that smoking caused Petitioner to develop RA.[14] *Id.*

Dr. Matloubian opined that some literature suggests that the elevated risk of RA from smoking may have to do with up-regulation of certain enzymes in the mucosa of the lungs, leading to production of citrullinated peptides. Tr. at 133. He opined that these citrullinated peptides break down immune tolerance in people with HLA-based susceptibility. *Id.* For this same reason, he opined, the literature suggests that there may be a link between periodontal disease and RA by way of the mucosa in the mouth. *Id.* at 134. He added that a third theory is that changes in the microbiome of the gut can also contribute to RA, but that more research is needed in this area. *Id.* at 135.

Dr. Matloubian opined that influenza virus is not considered to be a cause of RA. Tr. at 136. He added that influenza can cause inflammation in the lungs, but that this inflammation does not apparently lead to breakdown of immune tolerance. *Id.* at 137.

Dr. Matloubian next took issue with several of the environmental triggers that Dr. Brawer opined can lead to the development of RA. Tr. at 137. He opined that he was unaware of any link between severe emotional upset, pesticides and insecticides, hypoxia, hormonal imbalances, or prolonged exposure to unusual temperature changes and RA. *Id.* at 137-38. He agreed that there is a known link between streptococcal infections and rheumatic fever, as well as between campylobacter jejuni infection and Guillain-Barré syndrome. *Id.* at 138. He also opined that reactive arthritis can occur after chlamydia, urethritis, or infection with salmonella or shigella, but

[14] When asked to opine on Petitioner's smoking history as having been roughly half a pack per week rather than per day, Dr. Matloubian declined to say that this would have decreased or eliminated her risk of developing RA. Tr. at 171-72. He opined that there is a risk of developing RA even many years after a person stops smoking but conceded that the risk does decrease with time. *Id.* at 172.

opined that RA is not a post-infectious autoimmune disease. *Id.* Dr. Matloubian testified that, while certain infections, such as hepatitis B and C, are associated with inflammatory polyarthritis, this most often resolves within two to four weeks. *Id.* at 139. A diagnosis of RA, by contrast, requires six weeks of continuous symptoms. *Id.* He opined that influenza has not been associated with even transient inflammatory polyarthritis. *Id.*

Dr. Matloubian disagreed with Dr. Brawer's "perfect storm" theory of causation, opining that many of the factors Dr. Brawer pointed to, such as channelopathies, mitochondrial dysfunction, and toxins, have not been validated in the literature. Tr. at 141. He opined that this theory was "speculative and not established and not reliable." *Id.* He opined that, at any rate, there has been no evidence presented that Petitioner suffers from a channelopathy or mitochondrial dysfunction. *Id.* at 142.

Dr. Matloubian next gave his definition for molecular mimicry as the reaction of T and B cells to self-antigens as though they were foreign antigens. Tr. at 143. He opined that peptide sequence homology between self-antigens and foreign antigens is quite common, but that not all such homologies are biologically relevant. *Id.* That is to say, he opined, that not every instance of molecular mimicry causes disease. *Id.* Dr. Matloubian testified that "there's no evidence in the medical or scientific literature that there is molecular mimicry between influenza vaccine or virus-associated antigens and those antigens that are found to be associated with seropositive [RA]." *Id.* at 144. As support for this opinion, Dr. Matloubian added that researchers who study the pathogenesis of RA "use antigens derived from influenza virus as a negative control." *Id.* at 145.

Dr. Matloubian opined that, if molecular mimicry were to cause RA, that he would expect the time between exposure to the antigen and clinical symptoms would be about a week. Tr. at 145. This accounts for the time needed to produce a robust T and B cell response and for the T and B cells to travel to the site of inflammation. *Id.* at 145-46. He cited medical literature that argues that, if a vaccine can trigger an autoimmune condition via molecular mimicry, then the natural infection should be able to trigger that autoimmune condition as well. *Id.* at 147-48 (citing Ami Schattner, *Consequence or coincidence? The occurrence, pathogenesis, and significance of autoimmune manifestations after viral vaccines*, 23 VACCINE 3876-86 (2005) (filed as Ex. A, Tab 24) ("Schattner")). Dr. Matloubian argued that this phenomenon would need to be demonstrated by studies, not by case reports, in order to be credible. *Id.* at 148.

Dr. Matloubian reiterated his opinion that, based on the literature, there is no link between viral vaccines and autoimmunity. Tr. at 149. He also reiterated his point that the flu vaccine is recommended for patients with RA. *Id.* He explained that this is so because RA patients are frequently prescribed immunosuppressant medications, making flu infection more dangerous, and because "there's no risk to vaccines." *Id.*

Upon questioning by the Court, Dr. Matloubian opined that it is more likely than not that the synovitis and erosion noted prior to Petitioner's knee replacement surgery in November 2015 constituted the pre-clinical phase of her RA. Tr. at 180. He explained this by opining that osteoarthritis is a "bone-forming disease," meaning that, as cartilage wears away with age, osteoarthritis causes the bones to grow together. *Id.* at 180-81. By contrast, he continued, RA is a "bone-destroying disease" in which the profusion of profusion of the synovium erodes the bone.

Id. at 181. Dr. Matloubian testified that it is possible for a patient to have both osteoarthritis and RA at the same time. *Id.*

Dr. Matloubian opined that it is difficult to draw conclusions about the length of the lag time between onset of pre-clinical RA and clinical symptoms because it is rare for a patient to undergo blood testing for RA markers until symptoms of RA begin to appear. Tr. at 182. He testified that one exception was a study of military recruits who gave blood samples at multiple points over the course of their service. *Id.* Close relatives of patients known to have RA have also been tested and found to develop RA within three to five years of testing positive for anti-CCP antibodies. *Id.* at 183.

D. Post-Hearing Expert Reports

At the conclusion of the entitlement hearing, I requested an additional supplemental expert report from each party addressing synovitis and erosion and whether they are common findings in cases of osteoarthritis. Tr. at 202.

1. Dr. Brawer

In his seventh expert report, Dr. Brawer responded to my question, saying that the medical literature demonstrates that erosive changes occasionally occur in cases of osteoarthritis, but that this is not frequent. Ex. 53 ("Seventh Brawer Rep.") at 1. He opined that "[i]t is much more common for end stage Osteoarthritis to demonstrate synovitis," and noted that this is consistent with the November 5, 2015, pathology report of Petitioner's knee just before her knee replacement surgery. *Id.* He disagreed with Dr. Matloubian's testimony that Petitioner was suffering from seronegative[15] erosive RA in her knee prior to the flu vaccine, citing this same pathology report. *Id.* Dr. Brawer concluded by reiterating his opinion that Petitioner did not clinically manifest RA prior to her vaccination. *Id.*

2. Dr. Matloubian

In his third expert report, Dr. Matloubian responded to my question above. Ex. D ("Third Matloubian Rep.") at 1. He cited medical literature supporting the idea that erosion can occur in osteoarthritis, but that this is rare and restricted to the small joints of the hands. *Id.* (citing Doherty & Abhishek, *Clinical manifestations and diagnosis of osteoarthritis*, UP TO DATE (2021) (filed as Ex. D, Tab 1)). Dr. Matloubian opined that the medical literature does not support the occurrence of erosion in osteoarthritis of the knee. *Id.*

Dr. Matloubian concluded that Petitioner's medical literature also provides support for his previous hypothesis that Petitioner's knee replacement surgery may have been a physical trauma that triggered her RA. *Id.* (citing Julkunen; Al-Allaf, et al., *A case-control study examining the*

[15] Dr. Matloubian did not opine that Petitioner suffered from seronegative RA. Tr. at 122-23; First Matloubian Rep. at 7. Instead, Dr. Matloubian's opinion is that Petitioner developed RA prior to vaccination, and prior to her bloodwork that established her disease was seropositive.

role of physical trauma on the onset of rheumatoid arthritis, 40 RHEUMATOLOGY 262-66 (2001) (filed as Ex. 43) ("Al-Allaf")).

V. Applicable Law

A. Petitioner's Burden in Vaccine Program Cases

Under the Vaccine Act, when a petitioner suffers an alleged injury that is not listed in the Vaccine Injury Table, a petitioner may demonstrate that she suffered an "off-Table" injury. § 11(c)(1)(C)(ii).

In attempting to establish entitlement to a Vaccine Program award of compensation for a off-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274 (Fed. Cir. 2005). *Althen* requires that petitioner establish by preponderant evidence that the vaccination she received caused her injury "by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id.* at 1278.

Under the first prong of *Althen*, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Proof that the proffered medical theory is reasonable, plausible, or possible does not satisfy a petitioner's burden. *Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359-60 (Fed. Cir. 2019).

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). However, special masters are "entitled to require some indicia of reliability to support the assertion of the expert witness." *Boatmon*, 941 F.3d at 1360, *quoting Moberly*, 592 F.3d at 1324. Special Masters, despite their expertise, are not empowered by statute to conclusively resolve what are complex scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Hum. Servs.*, 121 Fed. Cl. 230, 245 (2015), *vacated on other grounds*, 844 F.3d 1363 (Fed. Cir. 2017); *see also Hock v. Sec'y of Health & Hum. Servs.*, No. 17-168V, 2020 U.S. Claims LEXIS 2202 at *52 (Fed. Cl. Spec. Mstr. Sept. 30, 2020).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position

to determine whether a 'logical sequence of cause-and-effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence also present in the record. *Hibbard v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 742, 749 (2011), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Caves v. Sec'y of Health & Hum. Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 Fed. App'x 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 F. App'x 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. Law Governing Analysis of Fact Evidence

The process for making factual determinations in Vaccine Program cases begins with analyzing the medical records, which are required to be filed with the petition. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Hum. Servs.*, 3 F.3d 413, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral

testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

Medical records created contemporaneously with the events they describe are generally trustworthy because they "contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions," where "accuracy has an extra premium." *Kirby v. Sec'y of Health & Hum. Servs.*, 997 F.3d 1378 (Fed. Cir. 2021) citing *Cucuras*, 993 F.2d at 1528. This presumption is based on the linked proposition that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Hum. Servs.*, No. 11-685V, 2013 WL 1880825 at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013).

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Hum. Servs.*, No. 03-1585V, 2005 WL 6117475 at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony -- especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; see also *Murphy v. Sec'y of Health & Hum. Servs.*, 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, there are situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Hum. Servs.*, 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475 at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Hum. Servs.*, 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent and compelling." *Sanchez*, 2013 WL 1880825 at *3 (citing *Blutstein v. Sec'y of Health & Hum. Servs.*, No. 90-2808V, 1998 WL 408611 at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *LaLonde v. Sec'y of Health & Hum. Servs.*, 110 Fed. Cl. 184, 203-04 (2013), aff'd, 746 F.3d 1334 (Fed. Cir. 2014). In making

a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. Analysis of Expert Testimony

Establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of her claim. *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594-96 (1993). *See Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (*citing Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592-95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora. *Daubert* factors are employed by judges to exclude evidence that is unreliable and potentially confusing to a jury. In Vaccine Program cases, these factors are used in the weighing of the reliability of scientific evidence. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted").

Respondent frequently offers one or more experts of his own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)). A "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly*, 592 F.3d at 1324. Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Id.* at 1325-26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations").

D. Consideration of Medical Literature

Although this decision discusses some but not all of the medical literature in detail, I reviewed and considered all of the medical records and literature submitted in this matter. *See Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally

presume that a special master considered the relevant record evidence even though [s]he does not explicitly reference such evidence in h[er] decision."); *Simanski v. Sec'y of Health & Hum. Servs.*, 115 Fed. Cl. 407, 436 (2014) ("[A] Special Master is 'not required to discuss every piece of evidence or testimony in her decision.'" (citation omitted)), *aff'd*, 601 F. App'x 982 (Fed. Cir. 2015).

V. Analysis

Because Petitioner does not allege an injury listed on the Vaccine Injury Table, her claim is classified as "off-Table." As noted above, to prevail on an "off-Table" claim, Petitioner must prove by preponderant evidence that she suffered an injury and that this injury was caused by the vaccination at issue. *See Capizzano*, 440 F.3d at 1320.

A. Causation in Fact/Significant Aggravation

Although Petitioner claimed in her petition that the flu vaccine significantly aggravated her condition, she did not pursue this argument in her pre-hearing or post-hearing briefs, or at the entitlement hearing. *See* Pet'r's Pre-Hearing Brief at 4 ("Elaine Clark asserts that the flu vaccine caused her Rheumatoid arthritis."); Pet'r's Post Hearing Brief at 3 ("Petitioner provided reputable medical and scientific explanation demonstrating that the flu vaccine caused her injuries."). Furthermore, Dr. Brawer testified multiple times that Petitioner did not have RA prior to receiving the flu vaccine. *See e.g.*, Tr. at 71, 101-02, 198. Accordingly, I have not analyzed Petitioner's case as a significant aggravation claim, and instead have considered it pursuant to *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274.[16]

B. Rheumatoid Arthritis Generally

RA is a chronic inflammatory disease characterized by inflammation of the synovium in multiple joints, leading to joint pain. Kraan at 1481. Without treatment, RA may lead to joint deformity and destruction. McInnes & Schett, *The Pathogenesis of Rheumatoid Arthritis*, 365 N. ENGL. J. MED. 2205-19, 2205 (2011) (filed as Ex. A, Tab 1) ("McInnes & Schett"). Its pathogenesis is not well understood, but genetic and environmental factors are thought to play a role. *Id.* at 2205-06. The two primary immune features of RA are rheumatoid factor and citrullinated autoantigens ("anti-CCP antibodies"). Malmström at 1. Patients with clinical symptoms of RA who test positive for both of these are diagnosed with seropositive RA, while those who suffer clinical symptoms of RA and test negative for these are diagnosed with seronegative RA. *Id.*

[16] Assuming Petitioner had advanced a significant aggravation theory, I find that theory would have been unpersuasive for the reasons articulated in this Decision. Namely, any significant aggravation theory would have necessarily relied on the same unpersuasive causal mechanism articulated in Petitioner's causation-in-fact claim. If Petitioner had pursued a significant aggravation claim further, it would be appropriate to discuss the legal standards for such a claim articulated in *Loving ex rel. Loving v. Sec'y of Health & Hum. Servs.*, 86 Fed. Cl. 135, 144 (2009). Because Petitioner abandoned this argument by not discussing significant aggravation in her briefs and because it is clear such as claim would fail, I have not analyzed this issue further.

RA is common, affecting about 1% of Caucasians. First Matloubian Rep. at 7. Women are about three times more likely than men to develop RA. *Id.* The parties agree that Petitioner was correctly diagnosed with seropositive RA. First Brawer Rep. at 2; First Matloubian Rep. at 6.

C. Persuasiveness of the Experts

While Dr. Brawer is qualified to offer his opinion as a rheumatology expert in this matter, several components of both his written expert reports and his testimony merit discussion.

Several times during his testimony, Dr. Brawer stated his opinion in sweeping terms without providing explanation or support. For example, he enumerated several factors in his "perfect storm" theory by saying

> It's clear that molecular mimicry may indeed be playing a role. It's clear that if you have a problem with a channelopathy, which I can explain, that may indeed factor in. It's clear that if you have a problem with regulatory T cells, that may also indeed factor in. And it's also clear that there's some participation by mitochondria in this process.

Tr. at 59-60.

In another example of this trend, Dr. Brawer opined that "[y]ou need a half a dozen things to come together to produce vaccine toxicity, and molecular mimicry is only one part of that. That's obvious to anyone who understands the diversity and heterogeneity of the vaccine toxicity as I've explained it." Tr. at 60. Dr. Brawer's repeated insistence on how "obvious" or "clear" his theory of causation was combined with his failure to fully explain that theory diminish the persuasiveness of his opinion.

In addition to overstating certain elements of his opinion, Dr. Brawer also misstated the age at which RA typically manifests. Dr. Matloubian testified that RA is a disease of older age, which typically peaks between the ages of 50 and 75. Tr. at 118. Dr. Brawer testified on redirect examination to rebut several of Dr. Matloubian's assertions; one of them concerned the age at which RA typically manifests. Dr. Brawer testified that: "Rheumatoid arthritis is a disease of young women, twenties, thirties, forties. Certainly we can see it in older age, but the peak incidence is in younger women." *Id.* at 187.

The medical literature supports Dr. Matloubian's testimony. *See, e.g.* Scott at 1097 ("Prevalence rises with age and is highest in women older than 65 years…"); Stanich at 181 ("RA can occur in individuals of virtually every age group, although the age of onset for a majority of the population is between 40–70 years. A US National Health Examination Survey (1960–1962) performed by Engel and colleagues showed the incidence of RA to be only 0.3% in adults younger than 35 years."); Crowson et al., *The Lifetime Risk of Adult-Onset Rheumatoid Arthritis and Other Inflammatory Autoimmune Rheumatic Diseases*, 63 ARTHRITIS & RHEUMATISM 3, 633-39 (2011) (filed as Ex. A, Tab 2) ("The cumulative risk was <1% before age 50 years, reflecting the small

incidence of RA at those ages. The cumulative risk of RA increased steeply in both sexes at ~60 years of age, where the incidence of RA was highest, and flattened after age 80 years.").

When asked twice on cross-examination whether he agreed with the statement from Crowson that the incidence of RA is highest at age 60, Dr. Brawer declined to answer the question. *See* Tr. at 189-92.[17] Dr. Brawer's testimony regarding this matter in conjunction with his broad statements regarding "clear" vaccination causation that were not further explained caused me to afford his opinion less weight than that of Dr. Matloubian.

D. *Althen* Prong One

In the context of the Program, "to establish causation, the standard of proof is preponderance of evidence, not scientific certainty." *Langland v. Sec'y of Health & Hum. Serv.*, 109 Fed. Cl. 421, 441 (2013). Petitioner's burden under *Althen's* first prong is to provide a medical theory causally connecting the vaccination and the injury. *Id.* This theory must be sound and reliable. *Boatmon*, 941 F.3d at 1359.

Petitioner is not the first to assert a causal relationship between the flu vaccine and RA in the Vaccine Program. My colleagues and I have consistently found that petitioners have failed to produce preponderant evidence that the flu vaccine can cause RA. *See Moran v. Sec'y of Health & Hum. Servs.,* No. 16-538V, 2021 WL 4853544 (Fed. Cl. Spec. Mstr. Oct. 4, 2021); *Hock v. Sec'y of Health & Hum. Servs.,* No. 17-168V, 2020 WL 6392770 (Fed. Cl. Spec. Mstr. Sept. 30, 2020); *Tullio v. Sec'y of Health & Hum. Servs.*, No. 15-51V, 2019 WL 7580149 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), *aff'd* 149 Fed. Cl. 448 (2020).

Petitioner initially contended that the flu vaccine caused Petitioner's RA because ingredients in the vaccine cross-reacted with self-antigens in her body, the phenomenon known as molecular mimicry. First Brawer Rep. at 2-3. While Dr. Brawer mentioned other possible mechanisms for how the flu vaccine could cause RA, his first expert report focused on molecular mimicry as a stand-alone theory. *See* First Brawer Rep. After I asked how molecular mimicry could begin within 24 hours of vaccine administration, Dr. Brawer then asserted that Petitioner's vaccination "triggered an immediate and brisk inflammatory response, manifested clinically by joint pain and stiffness." Fifth Brawer Rep. at 1. Dr. Brawer later elaborated on this theory, stating that molecular mimicry would not be enough on its own to cause Petitioner's RA. Tr. at 72-73. He theorized that several factors must co-occur, creating a "perfect storm" that enables a vaccine to cause autoimmune disease. *Id.* at 60. These factors include "regulatory T cell dysfunction,

[17] Dr. Brawer testified as follows: "You know, I'm glad you brought that question up because in order for you to understand current literature, you need to understand the old literature. And I understand the old literature because I lived through it, was trained through it, and I know it thoroughly. And I'm going to give a specific example and then I'm going to tie it to this case. I'll give two specific examples, but I'll be brief, Your Honor. The first has to do with drug-induced lupus, which appeared as a clinical entity in the early to mid-1970s. And if you look at textbooks from 45 years ago, you will find the statement by the person who was editing that particular chapter that most of the time systemic lupus that's drug-induced resolves when the drug is stopped, but not all the time. Sometimes the lupus persists. …" Tr. at 189-90. Although Dr. Brawer testified further along these same lines, he did not answer the question posed.

chemical toxicity, channelopathies, mitochondrial dysfunction, and what we call DAMPs, or damage-associated pathogens, molecular pathogens." *Id.* at 63.

According to Dr. Brawer, Petitioner experienced this inflammatory response on the same day as her vaccination. Fifth Brawer Rep. at 1. Dr. Brawer contended that this immunologic response became more widespread via "cellular proliferation and migration." *Id.* He added that "[s]ome of these vaccine-induced mechanisms may present themselves with acute arthritic phenomena within 24 hours. These phenomena then become accompanied by multiple slowly escalating amplification loops comprising other adverse immunologic responses that were also initiated on day one by the vaccination but did not become paramount and self-sustaining until several weeks later." *Id.*

For the reasons described below, I find that Petitioner has not provided a sound and reliable medical theory causally connecting the flu vaccine and RA.

1. Petitioner's "Perfect Storm" Theory Lacks Persuasiveness

I find that the "perfect storm" theory of causation articulated by Dr. Brawer at the entitlement hearing lacks persuasiveness.

The literature filed by both parties is all but unanimous in the conclusion that RA is a complex disease whose etiology remains unclear. *See, e.g.,* McInnes & Schett at 2205; Malmström at 14; Julkunen at 97; Brawer & Goel at 77. In his fifth expert report, Dr. Brawer opined that it is likely that multiple mechanisms of vaccine-induced disease operate at the same time, but that their effects are not necessary felt simultaneously. Fifth Brawer Rep. at 1. He elaborated on this thought at the entitlement hearing, when he testified regarding his theory of the "perfect storm," meaning that in order for a vaccine to trigger autoimmune disease, a host of different factors must also co-occur, including "regulatory T cell dysfunction, chemical toxicity, channelopathies, mitochondrial dysfunction, and what we call DAMPs, or damage-associated pathogens, molecular pathogens." Tr. at 63. He testified that the various factors result in "amplification loops" and that it may be the case that not all factors have equal clinical relevance at the start of the process. *Id.* at 64.

Dr. Brawer did not cite to any medical literature in his fifth expert report. During the hearing, he referred briefly to his own research and to his experience as a clinician to support the "perfect storm" theory. Tr. at 62, 64. He also conceded that this theory still needs to be validated in a research context. Tr. at 72.

In short, Dr. Brawer did little more than list a series of occurrences and mechanisms that he opines contribute to the "perfect storm." He did not describe how each event leads to the development or RA or how these events follow as a consequence of the flu vaccine. Dr. Matloubian testified that Dr. Brawer's theories are "quite speculative … and not reliable." Tr. at 141. I find that the lack of specificity as to each of the factors Dr. Brawer described undermine its persuasiveness.

According to Dr. Brawer, molecular mimicry plays a role in the induction of RA by the flu vaccine and is part of the "perfect storm." (*See* Tr. at 60, "You need a half a dozen things to come

together to produce vaccine toxicity, and molecular mimicry is only one part of that."). As with the other elements of the "perfect storm", Dr. Brawer did not further explain how the flu vaccine caused molecular mimicry resulting in RA.

It is well established in the Vaccine Program that, while the theory of molecular mimicry is generally considered to have some validity, a Petitioner must do more than invoke "the magic words 'molecular mimicry'" in order to satisfy the requirements of *Althen* prong one. *McGuinness v. Sec'y of Health & Hum. Servs.*, No. 17-0954V, 2021 WL 5292343, at *17 (Fed. Cl. Spec. Mstr. Oct. 20, 2021) (citing *McKown v. Sec'y of Health & Hum. Servs.*, No 15-1451V, 2019 WL 4072113, at *50 (Fed. Cl. Spec. Mstr. July 15, 2019)). Here, Dr. Brawer mentions molecular mimicry as a component of his theory of the "perfect storm," but he provides no further explanation. I recognize that petitioners are not required to demonstrate a specific biologic mechanism which caused their disease, nor are they required to present medical literature or epidemiological studies in support of their theory. *See Kottenstette*, 861 Fed. Appx. 433 (Fed. Cir. June 15, 2021) (citing *Knudsen*, 35 F.3d at 549) (reaffirming the principle that "proof of causation does not 'require identification and proof of specific biological mechanisms[.]'"); *Andreu,* 569 F.3d at 1378-79. However, a petitioner's prong one theory must be reliable. The mere mention of molecular mimicry, without more, does not constitute a reliable or persuasive prong one theory.

I note that in *Moran v. Secretary of Health and Human Services*, I previously considered whether the flu vaccine can cause RA via the theory of molecular mimicry. *Moran v. Sec'y of Health & Hum. Servs.*, No. 16-538V, 2021 WL 4853544 (Fed. Cl. Spec. Mstr. Oct. 4, 2021). I did not find that theory persuasive in *Moran*, and similarly do not find it to be so here.

In addition to the fact that Dr. Brawer has not done more than invoke the words "molecular mimicry", other evidence suggests that the flu vaccine does not cause RA via molecular mimicry. First, as Dr. Matloubian noted, evidence does not support that the flu *virus* causes RA. Tr. at 136. The medical literature supports this opinion. Stanich noted that "in no case has any single organism or group of organisms been demonstrated to be causative for RA." Stanich at 184. Schattner opines that in order for a viral vaccine to be established as a cause of autoimmunity, the viral infection should also be liked to autoimmunity. Schattner at 3881; *see also*, Noel R. Rose, *Negative selection, epitope mimicry and autoimmunity*, 49 CURRENT OPINION IN IMMUNOLOGY 51-55 (2017) (filed as Ex. A, Tab 27). According to Dr. Matloubian, "[t]he absence of a causal association between natural influenza virus infection and development of RA argues strongly against the possibility of molecular mimicry or bystander activation as a plausible biologic explanation." First Matloubian Rep. at 15. Dr. Brawer did not explain why the flu vaccine would cause RA but the flu virus has not been shown to do so. Instead, he opined that he has seen anecdotal situations where this has occurred. Tr. at 107.

Additionally, the Malmström article, which discusses the pathogenesis of RA, describes antigens from influenza virus as an "unrelated antigen" and use it as a negative control in their study. Malmström at 7. Dr. Matloubian described this as "a strong indicator that the general medical and research communities that study pathogenesis of RA do not recognize any relationship between RA associated antigens and those of influenza virus." First Matloubian Rep. at 13. I further note that in *Tullio*, the special master found this point to be a compelling argument against the applicability of molecular mimicry in a flu vaccine-RA case. He stated: "The view of these

experts that hemagglutinin is 'unrelated' to various rheumatoid arthritis associated proteins carries significant weight." *Tullio*, 2019 WL 7580149, at *21. I agree, and find this point is persuasive evidence which further undermines Petitioner's position that the flu vaccine caused Petitioner to develop RA via molecular mimicry.

2. The Majority of Persuasive Studies do not Support a Connection between Flu Vaccine and RA

Respondent sited several studies in support of his position that the flu vaccine does not cause RA. The overwhelming majority of the epidemiological evidence does not support a causal link.

Epidemiologic evidence is relevant with respect to *Althen* prong one. *See, e.g., D'Tiole v. Sec'y of Health & Hum. Servs.,* 2016 WL 7664475 (Fed. Cl. Spec. Mstr. Nov. 28, 2016), *mot. for review den'd*, 132 Fed. Cl. 421 (2017); *Blackburn v. Sec'y of Health & Hum. Servs.*, No. 10–410V, 2015 WL 425935, at *28–30 (Fed. Cl. Spec. Mstr. Jan. 9, 2015). However, this type of evidence is not required in order for a petitioner to establish that a vaccine can cause an injury. A vaccine injury is a rare event that cannot be disproved because a vaccinee did not experience a response consistent with that of the general population. *See Harris v. Sec'y of Health & Hum. Servs.*, No. 10–322V, 2014 WL 3159377, at *11 (Fed. Cl. Spec. Mstr. June 10, 2014) (finding that epidemiologic studies cannot absolutely refute causal connections, because it is possible that a larger study could always detect an increased risk), *mot. for review dismissed*, 2015 U.S. App. LEXIS 7921 (Fed. Cir. 2015).

In support of his position that Petitioner's RA was not caused by the flu vaccine, Dr. Matloubian cited Ray. First Matloubian Rep. at 10. This study involved a medical chart review of approximately one million patients in the Kaiser Permanente system from 1997 through 1999 and included both a cohort analysis and a case-control analysis. Ray at 6592. In Ray, the cohort analysis found a possible association between the flu vaccine and RA in windows approximately six months and one year after flu vaccination. *Id.* at 6596. The researchers in Ray then increased the power of the study and conducted a larger case-control analysis which concluded that there was no additional risk of developing RA after flu vaccination. *Id*. I find that the Ray study provides strong evidence that there is no association between flu vaccine and RA.

Dr. Matloubian also referred to the Bengtsson case-control study. First Matloubian Rep. at 10 (citing Bengtsson). This study followed 1998 cases of RA and 2252 controls for five years after vaccination. Bengtsson at 1831. Bengtsson found no association between the development of RA and prior vaccine exposure. *Id.* at 1832. Significantly, Bengtsson also found no increased risk of developing RA after vaccination in subjects who were smokers or who were carriers of HLA-DRB1 SE, the two best known risk factors for RA. *Id.* I find that this study also provides persuasive evidence that flu vaccine is not associated with RA.

Dr. Matloubian also cited Fomin, which assessed the safety of the flu vaccine in patients already diagnosed with RA based on data from 82 RA patients and 30 healthy controls. Fomin at 191. The authors of this study concluded that "[v]accination against influenza was not associated with a significant worsening of any clinical or laboratory index of disease activity." Fomin at 193.

I find that the absence of evidence that flu vaccination exacerbates pre-existing RA supports Respondent's position that the flu vaccine does not cause RA. The authors of the Westra article came to the same conclusion in their review of the literature. Westra, et al., *Vaccination of patients with autoimmune inflammatory rheumatic diseases*, 11 Nature Revs. Rheumatology 135-45 (2015) (filed as Ex. A, Tab 21) ("Westra"). This literature review reported on six studies which addressed the safety of the flu vaccine in patients with autoimmune rheumatic diseases, including RA. Westra at 140. The authors stated that "no significant influence of vaccination on disease activity has been reported." *Id.* at 140. Schattner came to the same conclusion in her literature review. Schattner at 3876 ("whenever controlled studies of autoimmunity following viral vaccines were undertaken, no evidence of an association was found.").

In addition, Dr. Matloubian cited Singh. Singh et al., *2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis*, ARTHRITIS & RHEUMATOLOGY, 1-25, 2015, (filed as Ex A Tab 22) (hereinafter "Singh"). Dr. Matloubian testified that the American College of Rheumatology concluded that the flu vaccine is recommended for people with RA. Tr. at 170; Singh at 17.

The totality of the literature submitted by Respondent persuasively demonstrates that there is not an association between the flu vaccine and RA.

Dr. Brawer submitted several medical articles in support of his position that the flu vaccine can cause RA. In contrast to Dr. Matloubian's references, Dr. Brawer relied primarily on case reports to support his theory. Brawer & Koyoda reported two cases in which patients experienced the onset of symptoms later diagnosed as RA within 24 hours of flu vaccination. Brawer & Koyoda at 1. Dr. Brawer also submitted Older, et al., which reports five cases of lupus erythematosus after various vaccinations. Older, et al., *Can Immunization Precipitate Connective Tissue Disease? Report of Five Cases of Systemic Lupus Erythematosus and Review of the Literature*, 23(3) SEMINARS IN ARTHRITIS & RHEUMATISM 131-39, 131 (1999) (filed as Ex. 29) ("Older"). Petitioner does not provide epidemiological evidence to support her contention that the flu vaccine can cause RA, and Dr. Brawer acknowledged that his theories still require validation in a research setting. Tr. at 72.

It is well established in the Vaccine Program that a petitioner is not required to provide epidemiological studies in order to satisfy prong one of the *Althen* analysis. *Capizzano*, 440 F.3d at 1325. Case reports can provide some limited support for a petitioner's theory of causation. *Campbell v. Sec'y of Health & Hum. Servs.*, 97 Fed. Cl. 650, 668 (2011) ("Case reports do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value compared particularly to formal epidemiological studies. Nonetheless, the fact that case reports can by their nature only present indicia of causation does not deprive them of all evidentiary weight."). Accordingly, I conclude that the case reports Petitioner filed do provide some support for her claim that the flu vaccine caused her RA. However, I find the epidemiological studies filed by Respondent more persuasive. I find that the weight of the evidence suggests that there is no association between the flu vaccine and RA.

Considering the totality of the evidence discussed above, I find that Petitioner has not presented a sound and reliable theory that preponderantly shows that the flu vaccine can cause RA. Petitioner has not satisfied the first *Althen* prong.

E. *Althen* Prong Two

Under *Althen's* second prong, a petitioner must "prove a logical sequence of cause and effect showing that the vaccination was the reason for the injury." *Althen*, 418 F.3d at 1278. The sequence of cause and effect must be "'logical' and legally probable, not medically or scientifically certain." *Id.* A petitioner is not required to show "epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." *Id.* (internal citations omitted). *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1325 (Fed. Cir. 2006). Instead, circumstantial evidence and reliable medical opinions may be sufficient to satisfy the second *Althen* prong. *Isaac v. Sec'y of Health & Hum. Servs.*, No. 08-601V, 2012 WL 3609993, at *16 (Fed. Cl. Spec. Mstr. July 30, 2012), *aff'd* 108 Fed. Cl. 743 (2013).

For the reasons outlined below, I find that Petitioner has not met her burden under *Althen* prong two.

1. Synovitis and Erosion

Of consequence to Petitioner's claim is the presence of synovitis and erosion in her left knee at the time of her knee replacement in November 2015. Ex. 11 at 45, 47. At the entitlement hearing, Dr. Brawer opined that these were the result of Petitioner's osteoarthritis and they do not indicate that she had RA prior to her flu vaccination on December 6, 2015. Tr. at 186. Dr. Brawer also opined that both synovitis and erosion occur in osteoarthritis, but that the latter is uncommon. Seventh Brawer Rep. at 1. Petitioner filed medical literature supporting this opinion. Mathiessen & Conaghan, *Synovitis in osteoarthritis: current understanding with therapeutic implications*, 19(18) ARTHRITIS RES. & THERAPY 1-9, 8 (2017) (filed as Ex. 40) ("Mathiessen & Conaghan") (stating that synovitis is commonly observed in osteoarthritic joints); Anandarajah, et al., *Patients with Erosive Osteoarthritis have Less Extensive Synovitis than Patients with Rheumatoid Arthritis on Histopathology*, Abstract No. 1112, ACR/ARHP Annual Meeting (2012) (filed as Ex. 38) ("Anandarajah") (concluding that synovitis occurs in both osteoarthritis and RA, but to a lesser extent in the former than in the latter); Punzi, et al., *Time to redefine erosive osteoarthritis*, 1 RHEUMATIC & MUSCULOSKELETAL DISEASES 1-2, 1 (2015) (filed as Ex. 37) ("Punzi") (showing that erosion is sometimes seen in cases of osteoarthritis, but only in the joints of the hands and spine).

Dr. Matloubian opined that synovitis and erosion are evidence that Petitioner had RA prior to receiving the flu vaccine. Tr. at 123. He testified that synovitis does occur in osteoarthritis, although less frequently than in RA, but that he would *not* expect to see erosion in osteoarthritis. *Id*. Dr. Matloubian also noted that none of Petitioner's literature mentions the "presence of erosive changes in knees of individuals with OA, which was the joint where Dr. Hoerner observed erosions intraoperatively in petitioner." Third Matloubian Rep. at 2.

Although the literature shows that synovitis and erosion can occur in osteoarthritic joints, Petitioner has not presented evidence that OA patients can experience erosions in joints other than the hands or spine. Because of this, the weight of the evidence supports the conclusion that it is more likely than not that Petitioner's synovitis and erosion resulted from her RA than from osteoarthritis. Thus, it follows that Petitioner's RA already existed at the time of her knee replacement roughly one month prior to receiving the flu vaccine. This finding is consistent with the extensive body of literature which describes a lag between the development of autoantibodies and the development of disease in RA patients. A petitioner cannot succeed on a claim of causation-in-fact where the alleged condition preexisted the vaccination. *See W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1354–55 (Fed. Cir. 2013) (affirming the special master's denial of compensation on claim of causation-in-fact because "[i]f a petitioner has a disorder before being vaccinated, the vaccine logically cannot have caused the disorder"). In this case, the medical records demonstrate that Petitioner was, more likely than not, experiencing symptoms consistent with RA at the time of her knee replacement surgery.

2. Lack of Evidence for the "Perfect Storm"

As discussed in the previous section, Dr. Brawer testified that vaccination can trigger autoimmunity leading to RA only when several factors coincide in what he referred to as a "perfect storm." Tr. at 62. These factors are molecular mimicry, "regulatory T cell dysfunction, chemical toxicity, channelopathies, mitochondrial dysfunction, and what we call DAMPs, or damage-associated pathogens, molecular pathogens." *Id.* Petitioner has not provided evidence that any of these factors were present at or before the onset of her RA.

3. Coincidental RA Onset After Vaccination

Dr. Matloubian opined that RA affects roughly 1% of the Caucasian population, with an incidence rate of roughly 40 for every 100,000 people. First Matloubian Rep. at 7. Respondent's medical literature supports the notion that RA is not a rare condition. Deane, et al., *Genetic and environmental risk factors for rheumatoid arthritis*, 31 BEST PRACTICE & RES. CLINICAL RHEUMATOLOGY 3-18, 4 (2017) (filed as Ex. C, Tab 2) ("Deane") (stating that RA affects 0.5% to 1% of the overall population); McInnes & Schett at 2205 ("[RA] is a common autoimmune disease."). Dr. Matloubian opined that the onset of Petitioner's RA shortly after vaccination is most likely a coincidence. First Matloubian Rep. at 14-15. In Ahmed, the authors found that, based on the general statistical likelihood of developing RA and the number of vaccine doses administered, there is a 90% chance of seeing one case of RA onset coinciding with vaccination for every 10,000 vaccine doses administered. Ahmed at 7. Dr. Matloubian opined that, "[t]aking into account that 150 million people are annually immunized with influenza in the U.S., we would expect then that 15,000 individuals would develop RA after such vaccination due to coincidence alone." *Id.* He concluded that, a woman's lifetime risk of developing RA being one in 28, Petitioner's RA was more likely that not unrelated to her flu vaccination. *Id.*

In the Vaccine Program, temporal association alone does not suffice to demonstrate causation. See, e.g., *Zumwalt v. Sec'y of Health & Hum. Servs.*, No. 16-994V, 2019 WL 1953739 at *20 (Fed. Cl. Spec. Mstr. Mar. 21, 2019), aff'd, 146 Fed. Cl. 525 (2019). The demonstrable

likelihood of symptom onset occurring after vaccination purely by coincidence cuts against Petitioner's argument.

4. Risk Factors for RA

It is relevant that the record shows that Petitioner had an elevated risk of developing RA due to factors unrelated to the flu vaccine.

First, Petitioner is a woman. Dr. Matloubian opined that RA is two to three times more common among women than men. First Matloubian Rep. at 7. Dr. Brawer did not refute this testimony.

Second, the record reflects that Petitioner smoked cigarettes for a period in the 1970s. Tr. at 132. The medical literature filed by both parties establishes that smoking is a known risk factor for RA. *See* Malmström at 2 (noting that smoking has a large impact on ACPA-positive patients); McInnes & Schett at 2011 (stating that "[s]moking and other forms of bronchial stress (e.g., exposure to silica) increase the risk of rheumatoid arthritis among persons with susceptibility HLA–DR4 alleles"); Hunt & Emery, *Defining populations at risk of rheumatoid arthritis: the first steps to prevention*, RHEUMATOLOGY, Vol. 10, 521-30, 2014 (filed as Ex. A, Tab 6) (observing that smoking is a risk factor for seropositive RA); Stanich at 187.

The strength of evidence that female sex and a history of smoking are known to elevate the risk of developing RA reduces the persuasiveness of Petitioner's argument that her RA was caused by the flu vaccine.

5. Treating Physicians

In weighing evidence, special masters are expected to consider the views of treating doctors. Cappizano, 440 F.3d at 1326. The views of treating doctors about the appropriate diagnosis are often persuasive because the doctors have direct experience with the patient whom they are diagnosing. *See McCulloch v. Sec'y of Health & Human Servs.*, No. 09-293V, 2015 WL 3640610, at *20 (Fed. Cl. Spec. Mstr. May 22, 2015).

Reviewing the medical record, I find some evidence that treating physicians may have attributed Petitioner's RA to the flu vaccine. Dr. Kohen, Petitioner's rheumatologist, noted on March 31, 2016, that "[t]here are descriptions in the literature of new onset inflammatory arthropathies after vaccinations, and since [Petitioner's] symptoms started after the flu vaccination, the vaccination could have been a contributory factor to the onset of her disease." Ex. 7 at 11. Dr. Matiello, Petitioner's neurologist, noted on November 1, 2017, that the medical literature contains case studies of small fiber neuropathy after flu vaccination and recommended that Petitioner not receive the flu vaccine that year. Ex. 10 at 6. In several years of medical appointments, suggestions by Petitioner's treating physicians that the flu vaccine may have caused her RA were rare and brief. Furthermore, neither medical provider described a mechanism for how the flu vaccine caused or contributed to Petitioner's condition.

The record also contains evidence that treating physicians did not attribute Petitioner's RA

to the flu vaccine. On March 24, 2016, Petitioner's pulmonologist, Dr. Coleman, stated that Petitioner "believes that the flu shot was the reason for those symptoms (which seems unlikely...)." Ex. 8 at 7 (ellipsis in original). Petitioner also had numerous appointments with providers who never noted any potential link between the vaccine and her RA. *See, e.g.*, Ex. 4 at 16 (appointment with regular physician, Dr. Gurka, on December 28, 2015); Ex. 6 at 39-43 (orthopedic follow-up on January 6, 2016).

Although I have considered them, treating physician statements that the flu vaccine "could have" been a contributory factor in the onset of Petitioner's RA, or that case studies show small fiber neuropathy can occur after the flu vaccine thus Petitioner should not receive her flu vaccine that year, do not constitute evidence sufficient for Petitioner to meet her burden. This is particularly true when viewed alongside her one treater who specifically described Petitioner's theory that the flu vaccine harmed her to be "unlikely". Accordingly, while I find that there is some support for Petitioner's claim in the opinions of her treating providers, I conclude that Petitioner has failed to preponderantly demonstrate that her flu vaccination was the cause in fact of her RA. Accordingly, she has not met her burden under prong two of *Althen*.

F. *Althen* Prong Three

The timing prong contains two parts. First, a petitioner must establish the "timeframe for which it is medically acceptable to infer causation" and second, he must demonstrate that the onset of the disease occurred in this period. *Shapiro v. Sec'y of Health & Hum. Servs.,* 101 Fed. Cl. 532, 542-43 (2011), *recons. denied after remand on other grounds*, 105 Fed. Cl. 353 (2012), *aff'd without op.,* 503 F. App'x 952 (Fed. Cir. 2013).

As to the medically appropriate timeframe, Dr. Brawer opined that Petitioner did not have RA prior to receiving the flu vaccine. Tr. at 71, 102-03. He opined that vaccine-induced RA may begin within 24 hours of vaccination but may take as long as three weeks to manifest. Fourth Brawer Rep. at 2. He added that "[t]rying to extend theories encompassing the idiopathic spontaneous onset of rheumatoid arthritis to its onset induced by varied environmental exposures is an exercise in futility." *Id.*

On the other hand, Dr. Matloubian opined that "it would be virtually impossible for an immune response to be initiated and cause symptoms within 24 hours and lead to all of her symptoms within 3-4 days as alleged by Dr. Brawer." First Matloubian Rep. at 13. He also testified that patients test positive for anti-CCP antibodies for up to 10 years prior to clinical onset, and three to five years on average. Tr. at 122 ("[S]eropositive RA…just doesn't start overnight…it's been going on for years before it becomes clinically apparent.").

The record contains significant evidence supporting the contention that RA develops over a much longer period of time than 24 hours to several days. Respondent presented evidence that the autoantibodies associated with RA are detectable in the blood up to several years before the disease is clinically apparent. Malmström at 2; Hazes & Luime, *The epidemiology of early inflammatory arthritis*, 7 NATURE REVS. RHEUMATOLOGY 381-90, 381 (2011) (filed as Ex. A, Tab 5); Hunt & Emery, *Defining populations at risk of rheumatoid arthritis: the first steps to prevention*, 10 NATURE REVS. RHEUMATOLOGY 521-30, 522 (2014) (filed as Ex. A, Tab 6); Nielen,

et al., *Specific Autoantibodies Precede the Symptoms of Rheumatoid Arthritis: A Study of Serial Measurements in Blood Donors*, 50(2) ARTHRITIS & RHEUMATISM, 380-86, 380 (2004) (filed as Ex. A, Tab 7); Kevin D. Deane, *Autoantibodies, citrullinated histones and initiation of synovitis*, NATURE REVS. RHEUMATOLOGY ONLINE (2015) (filed as Ex. A, Tab 13); Deane & Holers, *The Natural History of Rheumatoid Arthritis*, 41(7) CLINICAL THERAPEUTICS 1256-69 (2019) (filed as Ex. C, Tab 1) ("Deane & Holers").

Deane & Holers explain that, in light of the evidence that autoimmunity begins long before clinical symptoms of RA appear, "it is therefore highly likely that factors that trigger and propagate RA-related autoimmunity as well as drive the transition from pre-RA to [inflammatory arthritis] are acting years before a diagnosis." Deane & Holers at 1262. Deane & Holers do note that "not all individuals who develop [inflammatory arthritis] have detectable seropositivity for autoantibodies preceding their arthritis." *Id.* at 1265. They do state, however, that "existing studies suggest that a high percentage of individuals who develop [seropositive] RA will have seropositivity for these antibodies" before the onset of symptoms. *Id.*

I have already found that the synovitis and erosion present in Petitioner's left knee one month prior to vaccination were more likely due to ongoing RA than to osteoarthritis. Section (V)(E)(1), *supra*. Further, I have previously agreed with the reasoning of Chief Special Master Corcoran that

> given what is known about RA (and in particular the fact that the presence of the antibodies closely associated with it often long precede onset of RA symptoms), it is highly unlikely a vaccine could *either* cause these autoantibodies to develop in a medically-reasonable timeframe, or spark an autoimmune process dependent upon them, such that a vaccine administered close in time to appearance of RA symptoms could be deemed causal.

Moran, 2021 WL 4853544, at *35 (quoting *Monzon v. Sec'y of Health & Hum. Servs.*, No. 17-1055V, 2021 WL 2711289, at *19 (Fed. Cl. Spec. Mstr. June 2, 2021)). My opinion on this point has not changed. Petitioner has not presented preponderant evidence that 24 hours to several days is a medically acceptable timeframe for the onset of RA after flu vaccine, and thus has not established the third *Althen* prong.

VI. Conclusion

Upon careful evaluation of all the evidence submitted in this matter, including the medical records, the affidavits and testimony, as well as the experts' opinions and medical literature, I conclude that Petitioner has not shown by preponderant evidence that she is entitled to compensation under the Vaccine Act. **Her petition is therefore DISMISSED. The clerk shall enter judgment accordingly.**[18]

IT IS SO ORDERED.

[18] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by each filing (either jointly or separately) a notice renouncing their right to seek review.

s/ Katherine E. Oler
Katherine E. Oler
Special Master